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The Journal of Pediatrics

VOL. III OCTOBER, 1933 NO. 4

Original Communications

SIGNIFICANCE OF THE WATER METABOLISM IN HEALTH AND DISEASE

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INTRODUCTION

WERE we to decorate a map of the Western Hemisphere with pins representing the geographical distribution of individual contributors to the comparatively scanty literature on the topic of this evening's dissertation, it so happens that your own city would be the most densely pegged center before us. Because of this fact, I feel twice honored in having been invited to give this year's Packard Memorial lecture on the subject of water metabolism.

Unfortunately, the breadth of our subject will permit only the most superficial consideration of its many interesting phases. Certain subtopics admittedly of the greatest interest and importance, such as those relating to the mechanisms of edema formation and urinary secretions, will purposely be given less attention here than they deserve, because the readily available medical literature abounds in papers dealing with them. Whereas most treatises, dealing with the water exchanges of the body, direct attention primarily to other aspects of the metabolism and only secondarily to water, it will be my intention to reverse this order in the present discourse, purely for the sake of emphasis.

Although the broad science of metabolism had its very beginning in the experimental studies of Sanctorius of Padua (1561-1636) on the

From the Department of Pediatrics, University of Minnesota, Minneapolis.
The Annual Frederick Packard Memorial Lecture. Presented before the Philadelphia Pediatric Society, April 11, 1933.

"insensible perspiration," it is obvious to every one acquainted with the subject that progress in the field of water metabolism has lagged far behind that in other branches of physiology. The clinician has indeed long recognized the practical importance of water in certain disease states and has always credited it with a place among the essential constituents of the diet, but appreciation of its true significance in the body economy is only now beginning to manifest itself. That physiologists as a class have likewise failed in the past to give the problems of water metabolism their due recognition is evident from the fact that extensive investigations have not as yet been made with methods comparable to those which have so greatly advanced our knowledge regarding the intermediary metabolism of the proteins, fats, carbohydrates and minerals, and that concerning the vitamins and the total energy exchanges of the body.

Yet, if any single constituent of the living organism, or of the food which goes to maintain it, can be said to be the most important, water must be given that distinction, as attested not only by its quantitative position among the major constituents but also by the multiplicity of its essential physiologic rôles. Without water there can be no life, and for each organ there appears to be an optimal state of hydration for normal functioning. Whereas a mammal, such as the dog or man, may survive for a month or longer without all other food, losing practically his entire glycogen and fat stores and as much as half of his body protein, death may occur if he is deprived of water for longer than a few days, or when he has lost but little more than one-fifth of the water incorporated in his tissues. When it is remembered that the cells of the body are entirely dependent for their protection against the vicissitudes of the external world upon a delicately adjusted internal environment, characteristically watery in nature, the significance of the statement by Rubner that "the water content of the tissues is anxiously supervised by Nature," can be appreciated. As long ago as 1860 Claude Bernard, father of modern physiology, clearly expressed the importance of the fluid matrix when he said, "It is the fixity of the *'milieu interieur'* which is the condition of free and independent life" and . . . . "all the vital mechanisms, however varied they may be, have only one object, that of preserving constant the conditions of life in the internal environment."[1] Cannon[2] quotes Haldane as saying, "No more pregnant sentence was ever framed by a physiologist." We might add, that no more accurate expression of what our ultimate objective in therapeutics should be is likely ever to be made, because homeostasis or constancy of the body processes and materials is synonymous with health. Water is the most important single agent in making such constancy possible.

THE CHEMICAL NATURE OF WATER

A brief reference to the newer chemistry of water may fittingly be inserted at this point. It is no longer looked upon as being an inert substance consisting entirely of single molecules of H_2O, but is now thought by Armstrong[3] and others to be a mixture of such simple molecules and polymers of H_2O groups. According to this view, the higher the temperature the less becomes the degree of polymerization. So that, steam alone is looked upon as being H_2O, while ice is considered to consist of $(H_2O)_3$ and $(H_2O)_4$, and liquid water to be a mixture of H_2O, $(H_2O)_2$ and $(H_2O)_3$, the relative proportions of each form depending upon the temperature. The smaller open molecules are said to be chemically active, while the larger aggregates with closed groupings are inactive, as indicated in Fig. 1. The recent x-ray diffraction studies of water made by Stewart[4] may require some modifications of this conception of water and the still more recent synthesis of two

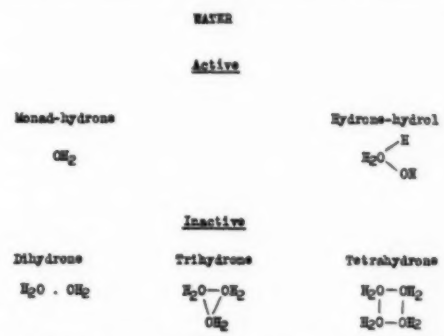

Fig. 1.—Assumed molecular constitution of water.

forms of water, heavy and light, by combination of the heavy isotopes of oxygen with the heavy isotopes of hydrogen and the light with the light, promises still further modifications. Nevertheless, the peculiar physical properties of water can be explained only on the basis of its being a mixture of molecules of different sizes and degrees of activity with spacial arrangements very different from those originally attributed to it.

THE PHYSIOLOGICALLY SUITABLE PROPERTIES OF WATER

This brief description of the chemical constitution of water, and an even more superficial consideration of its physical properties, will suffice to indicate why it is capable of entering into practically all of the regulatory processes of the living body and why nothing can take its place.[5] Its unique thermal properties, for instance, make possible the precise regulation of body temperature; its high surface tension serves all processes involving the phenomenon of adsorption, such as

the activity of enzymes; its high dielectric constant makes it a comparatively good insulator, while its matchless capacity as a solvent and ionization medium makes it an ideal vehicle for the transport of all essential materials to and waste products from the fixed cells of the body, as well as a medium for the innumerable chemical reactions which constitute life itself. That water plays more than a passive rôle in the body, however, is indicated by many facts and, as Mathews[6] points out, "the younger, the more vigorous, the more alive, the more actively growing, the more impressionable cells are, the more watery they are."

CONTENT AND DISTRIBUTION IN THE BODY

The percentage water content of the body varies inversely with age in man, as well as in other species. The human embryo is 97.5 per cent

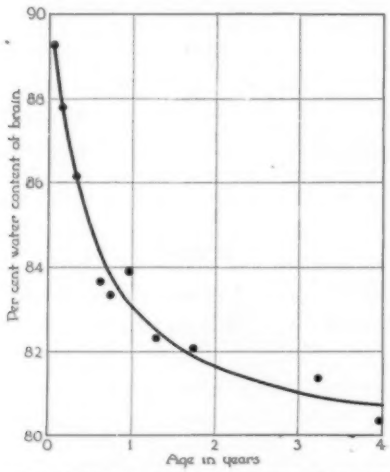

Fig. 2.—Relation of water content to age in a representative organ, the brain. (McQuarrie and Adolph.)

water at the sixth week of life. At the end of intrauterine life (birth) the percentage of water has decreased to between 71 and 72. Varying somewhat with the amount of fat present, the body of the adult contains between 58 and 65 per cent water. The true relationship of water content to age is best illustrated in a representative organ, like the brain, which shows a diminution in percentage of water with increasing age (Fig. 2). This difference in content undoubtedly explains in part the greater water requirement of infants and their greater susceptibility to the deleterious effects of dehydration. The percentage distribution of the water in the normal human body among the various organs has been shown by Volkmann[7] to be approximately that shown in Table I. In considering the water content from the

TABLE I

DISTRIBUTION OF WATER AMONG THE VARIOUS ORGANS (VOLKMANN)

Muscles	50.8 per cent	Brain	2.7 per cent
Skeleton	12.5 per cent	Lungs	2.4 per cent
Skin	6.6 per cent	Fat	2.3 per cent
Blood	4.7 per cent	Kidneys	0.6 per cent
Intestines	3.2 per cent	Spleen	0.4 per cent
Liver	2.8 per cent	Rest of body	11.0 per cent

practical point of view, however, it is more convenient to think of it as occurring in several compartments as defined by Gamble.[8] These are distinguished, not only by their situation within or outside the body cells or within closed vessels, but by their composition as well. The chief distinction between the intracellular fluid or cell sap, which constitutes the major portion of the body's water, and the extracellular fluids (lymph and blood plasma) is the greater concentration of colloids and of potassium and phosphorus compounds in the former and the greater mobility and greater content of sodium and chlorine in the latter. The extracellular or interstitial fluid, which occurs between the fixed cells, on the one hand, and the blood vascular bed on the other, differs in composition from the blood plasma chiefly in its lower content of colloids. Under conditions producing either dehydration or oversupply of water, it serves as an adjustable reservoir, which fluctuates in volume according to need. It serves thereby as a buffer depot, particularly for the plasma, resembling in this way, to use a simile of Cannon, a swamp, which may be drained during periods of drought but which becomes inundated during times of flood. When large quantities of isotonic NaCl solution were administered to dogs by Engels,[9] two-thirds of that retained was found to be stored in the muscle depots and one-sixth in the skin and subcutaneous tissues, showing these to be by far the most important reservoirs for storage of extra water. In all probability the bulk of the salt solution temporarily stored in the muscles under these conditions is taken up, not by the muscle cells themselves, but by the meshwork of connective tissue surrounding them.

Intracellular water is sometimes referred to as "living water" because it is incorporated in the cell as an essential constituent of the living protoplasm. Death follows its removal just as certainly as it would the removal of the protein or lipid fractions. In considering the significance of water as a constituent of the living organism, Gortner[10] illustrates this point as follows: "In most organisms a very considerable part of the growth process is nothing more or less than an imbibition of the bio-colloids. For example, a frog's egg, weighing on the dry basis only a few milligrams, can, after fertilization, be placed in a dish of filtered, sterile water and allowed to undergo the process of development. Such an egg will undergo cell division, giv-

ing rise at the end of several weeks to a living tadpole which may be as much as two centimeters in length and weighing several grams. Such a tadpole has never partaken of food other than utilizing the nutrients already present in the original egg and will be found on analysis to contain less dry matter than the original egg, due to the fact that a certain amount of the organic materials present have been utilized as a source of energy and eliminated as carbon dioxide and water. The growth during these several weeks has all been due to the intake of water which has become "living water," so the tadpole is actually more than 99 per cent water. It would be ridiculous to speak of this organism as being composed of only 1 per cent of vital materials. The water is as much a part of the tadpole as are the fats, proteins, et cetera, which serve to form the gel structure, and the biochemical and biophysical reactions which take place within the cells and tissues of the tadpole are determined probably more by the water which is present than by any or all of the other constituents."

Apparently the greater portion of the water of the body occurs in the free state, that is, in a mobile form which allows it to function as a solvent, as an interactant in chemical processes and as an agent for maintaining body temperature. Its location with reference to the body cells is evidently determined chiefly by the forces of osmosis and diffusion. The remainder occurs either in loose chemical combination with various other constituents or is held fast to the cellular or the circulating colloids by the physical force of imbibition. The equilibrium between these forms, free $\rightleftarrows$ bound, is probably involved in certain vital phenomena. For example, Balcar, Woodyatt and Sansum[11] have proposed a theory of fever based upon the assumption that a strong shift in the equilibrium toward the "bound" form, when tissue colloids are injured by toxins or other agents, produce a shortage in the supply of free water necessary for dissipation of heat, thus favoring a rise in the body temperature. Much work obviously remains to be done on this interesting phase of the subject before its real significance can be evaluated.[12]

ESSENTIAL ITEMS IN WATER BALANCE

When it is desired to evaluate the total water balance of the body for diagnosis or therapeutic purposes, a complete description can be obtained only by including the items shown in Table II. A fairly complete graphic representation of the total water exchange in a twelve-year-old girl subjected to various procedures influencing the state of hydration of the body is exemplified in Fig. 3, which is largely self-explanatory.

It is apparent from any set of data, showing the average values for these individual items, that the gains or losses of metabolic water may be very significant. Particularly is this so in the water balance of

young, rapidly growing subjects. A more detailed description of these particular fractions is shown in Table III. It is obvious from the latter data, indicating the extent of participation of water in the growth of tissue, why Kudo[13] and others[14, 15] have been able to maintain constant body weights in young animals, on otherwise adequate diets, by merely restricting their water intake. It is interesting to note that Kudo ob-

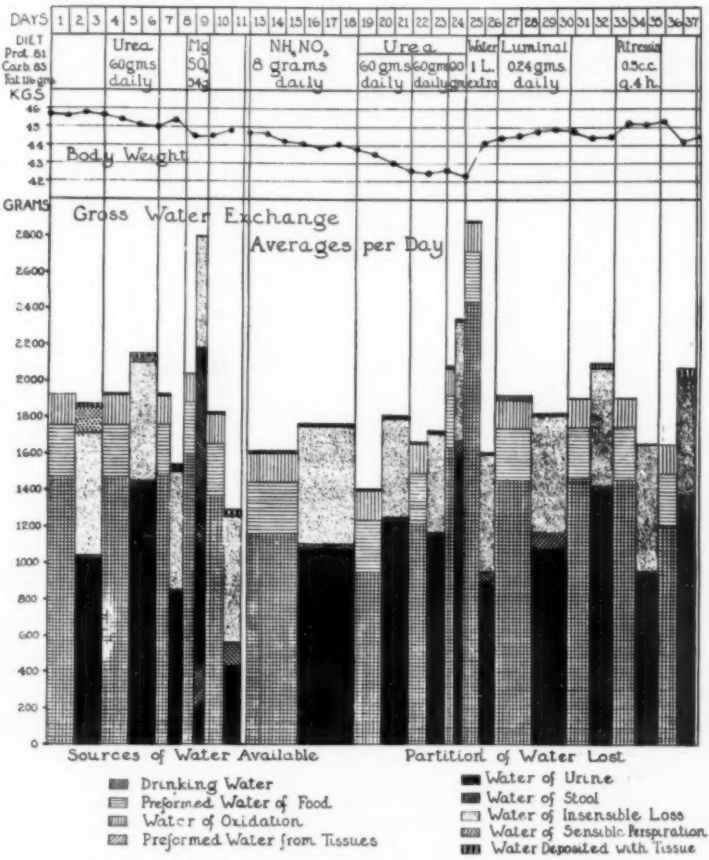

Fig. 3.—Graphic representation of separate items in water balance of body under various conditions. Constant diet. Thirteen-year-old girl. (McQuarrie, Manchester, and Husted.)

served an ability on the part of his experimental animals to adapt themselves to a greatly restricted water intake after being on such a regimen for some time. We have often made the same observation in the case of the human subject.

The magnitude of the oxidative formation of water within the body cells is shown in Table IV. Curiously enough, about 12 grams of water

is so formed on the average for each 100 calories, no matter what food is being oxidized. Babcock[16] has suggested that intracellularly formed water probably has greater value for the cell than water from the outside, because it tends to dilute the cell contents and so to draw nutritive substances into the cell by lowering the intracellular osmotic pressure. In the light of Armstrong's theory regarding the nature of water, Cathcart[17] further believes that this endogenous water may represent an active form specially suited for entrance into the metabolic activities of the body, whereas the circulating or "carrier" water may be composed largely of inactive molecules.

TABLE II

INDIVIDUAL ITEMS ENTERING INTO COMPUTATION OF THE WATER EXCHANGES OF THE BODY

WATER BALANCE OF BODY	
SOURCES OF WATER	DISPOSITION OF WATER
1. Water drunk (or injected).	1. Urinary loss.
2. Preformed water of food.	2. Fecal loss.
3. From oxidations in tissues.	3. Insensible loss from skin and lungs.
4. From syntheses and polymerizations in tissues.	4. Lost in sweat secretion.
5. Released from destruction of body tissues.	5. Deposited with new tissues.

TABLE III

RELEASE AND CONSUMPTION OF WATER IN THE COURSE OF CELLULAR ACTIVITY

METABOLIC WATER	
AVAILABLE SOURCES	HOW UTILIZED
1. From oxidations in tissues. e.g. $C_6H_{12}O_6 + 6O_2 = 6CO_2 + 6H_2O$	1. Combined in hydrolyses. e.g. $R\text{-}NH\text{-}COR + H_2O = R\text{-}NH_2 + R\text{-}COOH$
2. From syntheses in tissues. e.g. $R\text{-}NH_2 + R\text{-}COOH = R\text{-}NH\text{-}COR + H_2O$	2. Deposited with new tissue. e.g. 3 grams H_2O per 1 gram protein deposited. e.g. 0.2 grams H_2O per 1 gram fat.
3. Preformed water from destroyed tissues. e.g. 3 grams H_2O per 1 gram protein catabolized.	

The quantitative importance of the preformed metabolic water as a source during fasting or marked undernutrition is indicated by the fact that approximately two-thirds of the loss in body weight consists of water. The average amounts of preformed water occurring in some of the common foods are presented in Table V. Water drunk as such or that administered in isotonic solutions merely supplements these primary sources. The approximate amount of extra water needed for the complete metabolism of the food in an ordinary diet is indicated in Table VI.

Examples of the partition of water losses from the body in normal and atrophic infants are given in Table VII. It will be seen that under ordinary conditions approximately two-thirds of the output is by way of the kidneys and one-third by other pathways. Water lost in-

TABLE IV

WATER FORMED IN THE OXIDATIVE METABOLISM OF VARIOUS FOODS

	WATER FORMED PER 100 GRAMS	WATER FORMED PER 100 CALORIES
	c.c.	c.c.
Pure fat	107.1	11.5
Pure carbohydrate	56.0	13.8
Pure protein	41.3	10.3
Bread	33.0	12.9
Potatoes	11.2	12.2
Milk, cow's	8.2	12.2
Milk, human	8.7	12.3
Egg yolk	42.3	11.3
Egg white	5.5	11.4
Chicken, lean, cooked	15.3	11.2
Beef, medium fat, cooked	24.0	11.0

sensibly by way of the skin and lungs is a factor of the utmost practical significance, not only because of its relative magnitude as an item in the water balance, but also because, under standard environmental conditions (temperature range between 20° and 24° C. and relative

TABLE V

WATER CONTENT OF SOME COMMON FOODS USED BY INFANTS AND CHILDREN

FOOD MATERIAL	WATER CONTENT, PER CENT BY WEIGHT	WATER CONTENT, GM. PER 100 CAL.
Colostrum	85	119
Human milk	87	130
Cow's milk	87	130
Whole lactic acid milk plus 5 per cent sugar	82	97
Unsweetened evaporated milk	73	51
40 per cent cream	58	15
Butter	15	1
Cream cheese	34	82
Egg yolk	49	13
Egg white	86	156
Veal, leg	60	44
Beef, sirloin	54	25
Fresh ham	48	17
Fish, halibut	75	60
Bread, average white	36	14
Zwieback	5	1
Bananas	75	74
Potatoes	63	96
Spinach	83	220
Tomatoes	94	430
Carrots or beets	87	187
Orange	86	163
Apple	63	132

humidity between 30 and 60 per cent) and under circumstances not requiring strenuous muscular activity, approximately one-fourth of the heat produced in the body is dissipated in the process of its vaporization, as first shown by Soderstrom and DuBois.[18] On the basis of the latter fact, a fairly accurate gravimetric method for predicting the total heat production of the body has been developed by Benedict and Root[19] and further elaborated by Johnston and Newburg[20] and by Levine and his coworkers.[21] Correspondence between the average insensible loss (insensible loss = insensible water + CO_2 exhaled – O_2

TABLE VI

GRAMS OF WATER NEEDED FOR COMPLETE METABOLISM OF 100 CALORIES OF SOME FOOD SUBSTANCES

	PREFORMED WATER	GAINED BY OXIDATION	LOST IN DISSIPATING HEAT	LOST IN EXCRETING END PRODUCTS	DEFICIT
Protein	0	10.3	60	300	350
Starch	0	13.9	60	0	46
Fat	0	11.5	60	0	48
Beef, sirloin	25	11.3	60	119	143
Fish, cod	120	10.4	60	382	312
Eggs, hen	47	11.1	60	154	156
Milk, whole	127	12.5	60	123	43
Bread	14	13.2	60	69	102
Apples	150	13.9	60	56	–48

TABLE VII

PARTITION OF WATER OUTPUT IN INFANTS UNDER HOSPITAL CONDITIONS IN PER CENT OF TOTAL

URINE PER CENT	SKIN AND LUNGS PER CENT	FECES PER CENT	REFERENCE
60.0	33.5	6.5	Breast-fed (Rubner)
63.9	20.5	15.6	Atrophic (Rubner)
71.7	25.9	2.4	Bottle-fed (Niemann)
75.2	22.6	2.2	Atrophic (Bahrdt)

simultaneously inhaled) per hour and the total heat production per 24-hour period is sufficiently close to make possible reliable predictions from standard tables. An increase of one gram of insensible loss per hour is equivalent to approximately 32 calories in the 24 hours (Table VIII). In our own work we have found that the state of hydration of the body may influence the insensible water loss without significantly altering the total heat production, dehydration diminishing and superhydration increasing the output.[22] (See Table IX, Fig. 4.)

The percentage of the total body heat, which is dissipated by vaporization of water, rises rapidly with increasing environmental temperature. This rises from 17 per cent at 15° C. to 100 per cent when the environmental temperature equals or goes above that of the body.

Barbour[23] has shown that the first response of the body to a rise in the environmental temperature above the critical level for sweating (30° C.) is dilution of the blood by water mobilized from the tissues. While it is unlikely that this mechanism is in any way at fault in congenital ichthyosis, the absence of sweat glands in severe cases of this disorder greatly limits the ability of such persons to indulge in vigorous exercise or to withstand high temperatures. They tend to develop fever whenever the need for dissipating extra heat appears. Their insensible perspiration is, nevertheless, entirely normal.

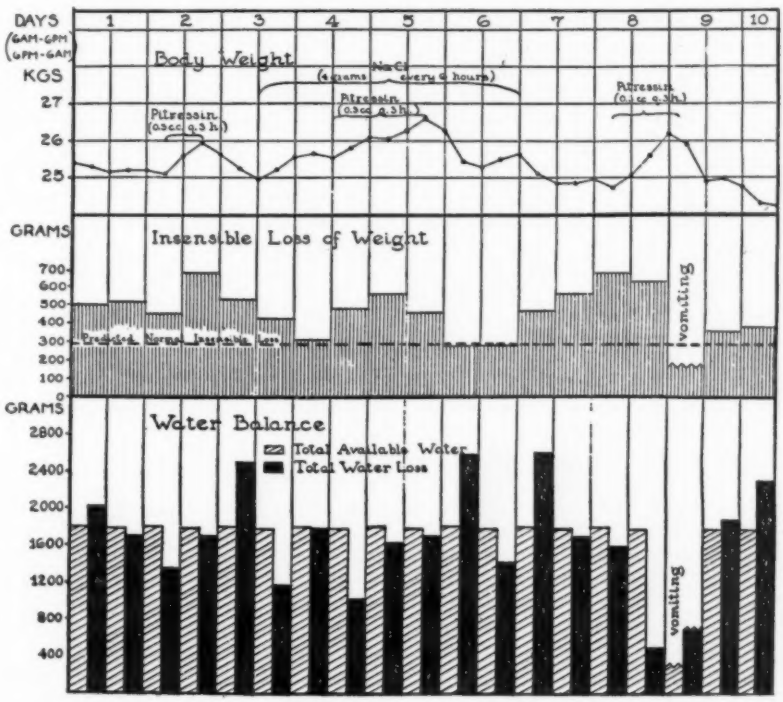

Fig. 4.—Effect of "superhydration," as produced by forced water drinking and pituitary antidiuresis, on insensible perspiration. Diet low in protein and minerals. Effect of added NaCl. Boy, aged nine years, wt. 26 kg. (Manchester, Husted and McQuarrie.)

WATER REQUIREMENTS OF THE BODY

The requirements of the body for water can now be estimated fairly closely if all significant conditions are known. They vary with such factors as age, muscular activity, temperature and humidity of the surroundings, type of diet and of course with the functional state of the various organ systems. The requirement in terms of age and size roughly parallels the total energy metabolism. It is, therefore, several times greater per unit of body weight during infancy than during

TABLE VIII

TWENTY-FOUR-HOUR HEAT PRODUCTION PREDICTED FROM THE HOURLY INSENSIBLE LOSS OF WEIGHT (MODIFIED FROM BENEDICT AND ROOT)

INSENSIBLE LOSS GRAMS	PREDICTED HEAT CALORIES	INSENSIBLE LOSS GRAMS	PREDICTED HEAT CALORIES
14.0	900	36.5	1606
14.5	916	37.0	1622
15.0	932	37.5	1638
15.5	948	38.0	1655
16.0	965	38.5	1670
16.5	981	39.0	1685
17.0	997	39.5	1700
17.5	1012	40.0	1715
18.0	1028	40.5	1730
18.5	1043	41.0	1745
19.0	1059	41.5	1760
19.5	1074	42.0	1775
20.0	1090	42.5	1791
20.5	1106	43.0	1807
21.0	1122	43.5	1823
21.5	1138	44.0	1840
22.0	1155	44.5	1855
22.5	1170	45.0	1870
23.0	1185	45.5	1885
23.5	1200	46.0	1900
24.0	1215	46.5	1916
24.5	1231	47.0	1932
25.0	1247	47.5	1948
25.5	1263	48.0	1965
26.0	1280	48.5	1980
26.5	1296	49.0	1995
27.0	1312	49.5	2010
27.5	1328	50.0	2025
28.0	1345	50.5	2040
28.5	1360	51.0	2055
29.0	1375	51.5	2070
29.5	1390	52.0	2085
30.0	1405	52.5	2100
30.5	1421	53.0	2115
31.0	1437	53.5	2130
31.5	1453	54.0	2145
32.0	1470	54.5	2161
32.5	1485	55.0	2177
33.0	1500	55.5	2193
33.5	1515	56.0	2210
34.0	1530	56.5	2226
34.5	1545	57.0	2242
35.0	1560	57.5	2258
35.5	1575	58.0	2275
36.0	1590	58.5	2291

adult life. The average amounts of water required by children of different ages under ordinary conditions are shown in Table X.

In vigorous muscular exercise the water requirement is raised by about three-fourths of one gram for each large calorie of extra heat so produced. With high environmental temperatures, such as occur in summer or even in winter in overheated nurseries, loss of water by way of the skin may double or even quadruple the ordinary requirements. From a combination of the two factors, strenuous muscular

TABLE IX

COMPARISON OF VALUES FOR HEAT PRODUCTION AS DETERMINED GASOMETRICALLY AND BY THE INSENSIBLE LOSS METHOD UNDER NORMAL CONDITIONS AND IN DEHYDRATION. INSENSIBLE PERSPIRATION AS ACTUALLY MEASURED AND AS PREDICTED FROM GASOMETRIC METABOLISM MEASUREMENTS COMPARED. J. R., AGED SIXTEEN YEARS, WEIGHT 48 KG. (FROM MANCHESTER, HUSTED AND MCQUARRIE.)

DIET (1712 CAL.)	MEAN ROOM TEMP. C.	MEAN RELATIVE HUMIDITY PER CENT	BODY WEIGHT KG.	NET CHANGE IN BODY WATER (GM.)	DEGREE OF DEHYDRATION	TOTAL CALORIES FOR PERIOD (12 HOURS)			INSENSIBLE PERSPIRATION FOR PERIOD (12 HOURS)		
						DET'D (TISSOT)	PREDICTED FROM INS. LOSS	PERCENTAGE DIFFERENCE	MEASURED	PREDICTED FROM TISSOT	PERCENTAGE DIFFERENCE
Borderline	24.0	70	47.41	0	None	659	657	− 0.3	326	327	− 0.3
Nonketogenic	22.0	73	46.55	−914	Moderate	639	580	− 9.2	266	312	−14.7
	23.0	66	47.60	+259	None	630	650	+ 3.2	319	310	+ 2.9
Ketogenic	22.5	54	46.62	0	Slight	672	654	− 3.2	322	340	−5.3
	22.5	58	45.36	−1308	Fairly Marked	666	560	−16.0	251	331	−24.1
High Protein	23.5	68	46.46	0	Moderate	693	614	−11.4	293	350	−16.3
	22.0	72	46.75	+300	Slight	694	630	− 9.0	303	350	−13.4
	22.5	61	45.42	−1233	Fairly Marked	664	500	−24.7	205	330	−38.0
	22.5	51	44.53	−2087	Fairly Marked	655	518	−21.0	220	324	−32.0
	23.0	50	43.90	−2572	Fairly Marked	639	508	−21.8	212	312	−32.0

activity and high external temperature, decrease in body weight, due almost entirely to loss of water by way of the skin and lungs, may amount to as much as 5 per cent in the course of three or four hours, unless an equivalent quantity of fluid, approximating in composition that which is lost, is taken in the meantime. Severe headache, abdominal discomfort, cramplike pains, muscle tremors and other symptoms of sodium chloride deficiency ("miners' cramp" or "stokers' disease") ensue, if water alone is taken to quench the thirst after excessive loss of water from sweating.[24]

Obviously, diseases accompanied by profuse vomiting or diarrhea demand an increase in water intake in proportion to the amount so lost. The possible magnitude of losses by the latter routes is indicated by the comparatively enormous amount of fluid secreted into and absorbed from the alimentary tract in the course of 24 hours even under normal conditions (Table XI). These amounts may be greatly exceeded in the case of active diarrhea.[25] Unless the particular mineral elements which are lost in such secretions are quantitatively replaced along with water, the fluid matrix of the body cannot be adequately repaired.[20] Prolonged acidosis of the type occurring in neglected cases of diabetes mellitus results in a serious deficit of water and fixed base, which requires a type of replacement similar to that indicated in diarrhea. Since the rate of metabolism increases approximately 13 per cent for each degree centrigrade rise in body temperature, fever greatly increases the water requirement for dissipation of extra heat produced.

The nature of the diet or the metabolic mixture influences the water requirement very decidedly. Even during a fast the minimum amount of water necessary for excretion of nonvolatile waste materials is considerable. Obviously the greater the quantity of mineral salts in the diet and the greater the amount of protein catabolized the greater will be the volume of water necessary for excretion of ash and nitrogenous end products. Gamble, Putnam and McKhann[27] found that, when two millimols of NaCl, KCl, $KHCO_3$ or urea per gram of food was added to the diet of rats, an approximately stationary concentration in terms of water intake was established. The values for NaCl were 0.63 molar and for urea 1.01 molar. The optimal water requirement for all salts was identical, or nearly so, and for salt mixtures the requirement tended to be additive. For mixtures of salts and urea the requirement was not additive, but the same as for an equivalent amount of urea alone.

It goes without saying that the amount of water necessary for general body well-being in the untreated case of diabetes insipidus is the highest known. For instance, we have in our metabolism ward at the present time a four-year-old boy with diabetes insipidus, who has a

total daily water exchange of between seven and eight kilograms and gives the history of having passed as much as four gallons or about 16 kilograms of urine in one day, although his present body weight is only 11 kilograms. The mechanism of this disorder is discussed at greater length below.

Adolph[28] has summarized the coefficients for calculating the water requirements of an essentially normal individual in c.c. per 24 hours, from the surface area of the body (in sq. m.) and the total caloric

TABLE X

RANGE OF AVERAGE WATER REQUIREMENT OF CHILDREN AT DIFFERENT AGES UNDER ORDINARY CONDITIONS

AGE	AVERAGE BODY WEIGHT IN KILOS	TOTAL WATER IN 24 HOURS	WATER PER KILO BODY WEIGHT IN 24 HOURS
3 days	3.0	240–300	80–100
10 days	3.2	400–480	125–150
3 months	5.4	750–864	140–160
6 months	7.3	950–1,130	130–155
9 months	8.6	1,075–1,240	125–145
1 year	9.5	1,140–1,300	120–135
2 years	11.8	1,350–1,475	115–125
4 years	16.2	1,600–1,800	100–110
6 years	20.0	1,800–2,000	90–100
10 years	28.7	2,000–2,440	70–85
14 years	45.0	2,250–2,700	50–60
18 years	54.0	2,160–2,700	40–50

TABLE XI

AVERAGE RATES OF SECRETION OF DIGESTIVE FLUIDS IN ADULT MAN (ROWNTREE)

SECRETIONS	AMOUNT C.C.	AUTHORITY
Saliva	1500	Bidder and Schmidt
Gastric juice	2000 to 3000	Bidder and Schmidt
Bile	300 to 500	Pfaff and Balch
Pancreatic juice	500 to 800	Wohlgemuth
Succus intericus	3000	Pregl
Approximate Total	8000	

requirements (in large cal.) as shown in Table XII. While this is obviously not a precise practical method, it serves to emphasize the approximate magnitudes and the range of variations in the requirements.

REGULATION OF WATER CONTENT AND EXCHANGES

Fortunately, the body has more or less automatic mechanisms for maintaining an optimum content of tissue water. Thirst, which is apparently a sensation dependent upon some degree of deficit in the free water of the salivary glands and mucous membranes of the mouth,[29] is usually a trustworthy indicator of the body's need for water. Little concern need be felt regarding the possibility of a person's taking too much water excepting in a very limited number of

pathological states which will be referred to later. Extra water taken, if unaccompanied by sodium chloride in or near isotonic concentration, is fairly promptly excreted by the kidneys with but little effect upon the general body metabolism. While the mechanism of this water diuresis is not perfectly understood, Marx[30] claims that the blood is diluted shortly after water is drunk, and to almost the same extent whether the amount taken is 1000, 500 or as little as 50 c.c. Because of the latter fact he assumes that the intake of water starts a complicated chain of reactions between the blood and the tissues, involving the whole mechanism of water metabolism and finally resulting in diuresis of the excess water. That dilution of the blood results in the calling into activity of an increased number of renal glomeruli is indicated by the work of Richards.[31] The influence of a nervous or

TABLE XII

COEFFICIENTS FOR CALCULATING THE WATER REQUIREMENT OF AN INDIVIDUAL, IN C.C. PER 24 HOURS, FROM THE SURFACE AREA OF THE BODY (A) AND THE CALORIC REQUIREMENT (E)

Growth	0	15 A	30 A
Basal urinary	400 A	1,000 A	1,500 A
Basal fecal	30 A	90 A	150 A
Basal extrarenal	250 A	390 A or	
Exercise (sweat)	1.73 × 0.4 E	1.73 × 0.25 E basal 1.73 × 0.55 E exercise	
Temperature (sweat)	----------	1,800 A (C −32)	
Total (approximate)	2,100	3,400	5,000

psychic factor has also been demonstrated by Bykow and Berkman[32] and by Marx,[33] who found that blood dilution occurred in trained dogs through the mechanism of conditioned reflexes without the administration of extra water and in a hypnotized man following mere suggestion of water drinking.[34] When isotonic NaCl solution is taken instead of water, there is but slight diuresis and blood dilution persists longer. Comparatively enormous amounts of water may be stored in the extracellular reservoirs of the body without harm, if it is given in the form of Ringer's solution.

Administration of excessive amounts of tap water (50 c.c. per kg. per hour) to normal animals was found by Rowntree and his coworkers[35] to produce a symptom complex which they designate as "water intoxication." This syndrome consists of restlessness, muscle tremors, vomiting, diarrhea, incoordination, prostration, generalized convulsions and finally death, if water administration is continued. These signs are much less severe or do not develop at all, however, if physiological saline solution is given instead of tap water. Snell and Rowntree[36] described the case of a man with severe diabetes insipidus with compulsion thirst, who developed these symptoms spontaneously on

several occasions when he drank enormous quantities of tap water (20 quarts in twenty-four hours). In collaboration with Thompson and Johnson, the author has recently had the opportunity to study the water and mineral balances in a child with diabetes insipidus who repeatedly had convulsions when a small excess of water was stored following pitressin administration. Miller and Williams[37] produced asthenia, muscle cramps, headache, dizziness and elevated blood pressure, but no convulsions, in a human subject, when they administered 10 quarts of water directly into the duodenum by Rehfuss tube. The body weight of this subject was increased from 124 to 142 pounds in a period of twelve hours. Harding and Harris[38] found 10 per cent NaCl to be the most efficient antidote for "water intoxication." Rowntree[39] attributes the symptoms to a disturbance of the normal balance between the various electrolytes of body fluids. Smyth and coworkers[40] from a more recent study of the mechanism involved, conclude that the essential cause of the convulsions is alkalosis due to loss of gastric Cl.

According to the investigations of Lamson and Roca[41] and of Pick[42] and his coworkers the sequence of events resulting from the liberal administration of fluid in the normal subject is as follows: The liver acts as a temporary reservoir for a considerable portion of the excess water taken, thus preventing sudden overloading of the right side of the heart. The liver then diminishes in size gradually as the stored fluid escapes into the general circulation by way of the lymphatics. In the normal dog diuresis from water ingestion was found by Molitor and Pick[42] to begin not earlier than 50 to 60 minutes after water was given and lasted for three or four hours, while in the dog with an Eck fistula (which largely excludes the liver from the circulation) extra water began to appear in the urine within 20 to 30 minutes and the diuresis required but half the normal time for its completion.

The mechanism by which the liver performs this function as a temporary reservoir is apparently as follows: Through the reflex activity of the sympathetic vasomotor system (as confirmed by adrenalin injections), constriction of the hepatic veins and closing of their valves follows the ingestion of the fluid, thus causing partial obstruction to the outflow from the liver. Simultaneously with this, the pressure in both the hepatic artery and the portal veins increases, causing thereby increased filtration pressure in the liver capillaries with gradual outflow of water into the lymph spaces and finally into the thoracic duct. Excess water taken as such is then fairly promptly excreted by the kidneys, whereas isotonic NaCl solution is secondarily stored for a longer time in the extracellular depots of the body, particularly in the muscles and skin, as previously pointed out. In liver disease this temporary storage function is said to be impaired, as indicated by greater dilution of the blood following water administration.[42]

INTERCHANGE OF WATER THROUGH LIVING MEMBRANES

Revolving around the problem of edema, much study has been devoted in recent years to the mechanism of interchange of fluid between the blood capillaries, on the one hand, and the lymph or tissue spaces (intercellular reservoir), on the other. Since the subject has been adequately summarized in recent papers by Leiter,[43] Landis[44] and others, however, little need be said of it here excepting to enumerate the chief factors concerned. Starling's[45] original claim, that the outflow of fluid from the capillaries is dependent upon the hydrostatic pressure of the blood within them and that the inflow from the tissues is dependent upon the colloidal osmotic pressure of the plasma, has been adequately substantiated, i.e., when the hydrostatic pressure at the venous end of the capillaries is greater than the osmotic pressure of the plasma proteins, edema will occur. Colloidal osmotic pressures below 19 to 20 mm. of mercury,[46] corresponding with a total plasma protein range below 5.5 ± 0.3 per cent or a plasma albumin range below 2.5 ± 0.3 per cent or plasma specific gravity below 1.022,[47] favor the occurrence of edema. As pointed out by Landis and others, there are undoubtedly additional factors of importance, particularly under abnormal conditions. Chief among these factors are tissue pressure, amount of protein which has escaped into the fluid outside of the capillaries, local temperature and state of oxygenation of the blood. Injury of any kind to the capillary walls results in increased permeability not only to water and simple crystalloids but to plasma proteins and lipids as well. Many of these factors are undoubtedly involved also in the passage of fluids through the epithelial as well as the endothelial cells in the special organs, such as the kidneys, the cerebrospinal system, the gastrointestinal tract and various purely secretory structures, but much still remains to be learned regarding the exact mechanisms of transfer in these complicated systems.

The factors regulating exchange of water between the intracellular and the extracellular compartments have not been studied extensively, although they are undoubtedly of the utmost importance to the organism. In addition to certain of those enumerated above, there are unquestionably others to be considered, such as the different mineral patterns of the fluids on the two sides of the cell membrane, the acid base equilibrium, the type of metabolic process predominating within the cells, the physicochemical peculiarities of the cell colloids and membranes, and lastly certain extrinsic nervous and endocrine factors. Considered in this light, it is obvious that cellular activity must be accompanied by continuous changes in the water distribution between the cells and their immediate environment.

EFFECTS OF VARIOUS IONS

While any shift in the acid-base equilibrium of the body fluids toward the alkaline side appears to favor the retention of water by the tissues,[48] the Na ion, in contrast with all others, appears to be more or less specifically active in this regard. While Br behaves very similarly to Cl, attempts to replace Na by other cations, as for instance K, usually results in water loss rather than storage. A shift of the acid-base balance toward the acid side results in loss of body water. The action of mineral acids and acid-forming salts, such as NH_4Cl, $CaCl_2$ and NH_4NO_3, is similar to that of the ketogenic type of acidosis and the acidosis of severe diarrhea, in causing a loss of body water. While increase in the H-ion concentration *per se* may be important because of its direct influence on the capacity of the colloids to hold water, the loss of Na which occurs under such conditions is probably the more potent factor. Fenn[49] has recently found that K migrates into or from muscle cells in company with OH and not with other anions. Potassium, therefore, tends to shift from an intracellular to an extracellular position when the OH concentration within the cell is greater than that in the fluids outside of the cell. The direction is reversed when the pH of the extracellular medium is higher than that of the cell fluid. Presumably water translocation accompanies such shifts. Haldi and his coworkers[50] in a study of the factors affecting hydration of nervous tissue in vitro found that different parts of the brain swell to a certain degree when placed in distilled water. They then found that the anions of various K salts inhibit water absorption by the tissues in the following order: citrate> tartrate> oxalate> SO_4> acetate> CNS> Br> NO_3> Cl> I. In the cation series the bivalent ions were found to inhibit swelling more effectively than monovalent ions. The cations of Cl inhibited the taking up of water as follows: Ca, Ba, Sr> Na, Li> K, Cs, Rb.

INFLUENCE OF DIET

Beyond the facts, first, that a minimum amount of water is required for the excretion of the nonvolatile end products of catabolism (100 c.c. for every 4.5 grams urea and 65 c.c. for each gram of ash), second, that prolonged protein deficiency causes water retention secondary to the lowering of the plasma protein content, and third, that ketogenesis promotes loss of body water, as already indicated, the dietary has but little influence on water regulation. The claim that carbohydrate *per se* has a specific water-retaining effect has not, to my knowledge, been adequately substantiated by uncomplicated experimentation. The impression, that a high carbohydrate diet results in storage of excess water in the tissues, probably originated from observations made on so-called hydrolabile infants and older subjects suffering from genuine

nutritional edema. It has been well established that the vast majority of such patients retain water because of the low plasma protein which results from a deficiency of protein in the diet. It is probably true that the edema found in the "moist" type of beriberi is explainable on the same basis.[51] Of course, carbohydrate has a specific effect in checking the excessive water loss due to the ketogenic type of acidosis merely by virtue of its effect in counteracting ketogenesis.

RÔLE OF PHOSPHOLIPIDS AND CHOLESTEROL

That the balance in the tissues between the physiologically antagonistic substances, cholesterol and lecithin, may be an important factor in water metabolism is indicated, not only by the fact that the former is lyophobic and the latter lyophilic, but even more directly, by the finding of Degkwitz[52] that cholesterol administered parenterally results in active diuresis while lecithin causes water retention. Dahmlos and Solé[53] found that lecithin and OH^- together favor an oil in water dispersion system, while cholesterol and H^+ are antagonistic to the formation of such a system. They, therefore, conclude that lipids constitute a very important factor in the penetrability of membranes by water and electrolytes. Cholesterol injected intravenously was found by these authors also to cause temporary hydremia and an increase in plasma Cl which resulted later in an increased output of both water and Cl in the urine. Lecithin is reported to have had an opposite effect. In this connection it is interesting to note that Haustein[54] found the serum cholesterol to be low in a series of hydrolabile children.

ENDOCRINE AND NERVOUS FACTORS

The most important extrinsic factors in the regulation of the water metabolism are the interrelated endocrine and nervous influences. Of the former, the secretion from the posterior lobe and pars intermedia of the pituitary body is unquestionably the most potent. This was first discovered in 1901 by Magnus and Schafer,[55] who found it to have a diuretic action when injected into the anesthetized animal. Not until 12 years later was its more important antidiuretic action in the unnarcotized subject discovered by von den Velden.[56] In a heart-lung-kidney preparation made in such a way that the pituitary body could be inserted at will, Starling and Verney[57] found that the effect of its presence in the circuit was to interrupt the flow of urine. They observed in a similar preparation that the antidiuretic activity following pituitary extract was accompanied by an increased chloride excretion.[58] Motzfeldt[59] first proved its antidiuretic effect during polyuria due to oral administration of large quantities of water, while von den Velden demonstrated its effectiveness in stemming the flow of urine in diabetes insipidus when injected subcutaneously. Blumgart[60] later found that it is just as efficient in controlling the polyuria of diabetes

insipidus when sprayed intranasally as when given by hypodermic injection. In a special study on the diphasic action of pituitrin McFarlane[61] found that high-speed intravenous injection, like light ether anesthesia, tends to favor a diuretic response, while slow intravenous injection inhibits urinary flow.

McQuarrie and Peeler[62] made the observation that there is a significant net loss in body weight following a period of sustained pituitary antidiuresis when the subject is on a low-mineral, high-water intake. Thompson, Ziegler and McQuarrie[63] have found this procedure to be effective in reducing certain types of edema. In several instances the equivalent of the well-known "spontaneous diuresis" has apparently been initiated by the procedure, when the level of the serum proteins at the time of the test was not far below the critical point for edema formation. This weight-reducing effect is apparently dependent upon the extra excretion of salt during the period of antidiuresis.

The mechanism by which this hormone produces antidiuresis is still the subject of controversy, some workers believing that it acts directly on the renal mechanism, others that it affects the other tissues of the body primarily. The latter observers consider that the kidneys function in a purely secondary manner in response to changes in the blood circulating through them. It seems highly probable that the action is a complicated one involving both the kidneys and the general body tissues simultaneously. Richards and Plant[64] found by direct observation that the first response to the extract was constriction of the efferent glomerular vessels, which produced a temporary diuresis, while a later more striking response was constriction of the afferent vessels, which resulted in antidiuresis. According to Geiling,[65] increased reabsorption from the kidney tubules, resulting from a specific effect of infundibular extract on the tubular epithelium, may be largely responsible for the antidiuresis. Marshall[66] has recently obtained convincing evidence that the loop of Henle may be the chief site of antidiuretic action in the kidney. Excretion of potassium chloride, urea and other substances given by mouth with one liter of water was found by Adolph and Ericson[67] not to be inhibited by intramuscular injections of pituitrin. These authors found that the amount of water excreted under these conditions was limited to that for removing the excess salt, the remainder being retained. They concluded that the extract acts by rendering the kidneys insensitive to excess water in the blood plasma.

That pituitrin affects other tissues as well as the kidneys is indicated by the finding that salivary, gastric and intestinal secretions are inhibited by its injection.[65, 68] At the same time lymph flow decreases and its protein content increases. Hydremia and mobilization of electrolytes from the tissues into the blood stream occur following injection of pituitary extract, even after bilateral nephrectomy.[68] Stehle,[70]

finding an increased urinary excretion of various salts during antidiuresis, concluded that the effect of pituitrin is to mobilize electrolytes into the blood and in so doing renders the tissues capable of taking up more water. On the basis of this, he advances the theory that in diabetes insipidus the failure of the body to retain water is due to a reversal of the electrolytic conditions found in the tissues when pituitary extract is administered. Barbour and his associates[71] found an increase in the water content of the cerebrum, medulla and basal ganglia and in the muscles and liver, following pitressin injection, whereas they found a decrease in the skin and subcutaneous tissues. From water vapor studies by Hill's method, it was found by Barbour that water administration tended to produce less of an osmotic pressure fall after pituitary extract than it did in the absence of this substance. Yet the blood specific gravity fall was decidedly greater. The author interprets this as an indication that the pituitary hormone causes mobilization into the blood of a slightly hypertonic salt solution. He concludes that the kidney is tending to assume a minor rôle as a primary locus of water shifting after pituitary administration.

Glass,[72] who likewise found the water content of striated muscle markedly increased by injection of pituitary extract, considered this control of tissue swelling by pituitrin to be dependent upon nerve action because sympathectomy as well as extirpation of the centers of the midbrain markedly affected the water content of the muscles. Hypertonic solutions interfere with the hypophyseal influence on tissue swelling by preventing escape of plasma water to the tissues. According to Janssen,[73] section of the spinal cord at the level of the fifth cervical interspace does not interfere with the action of posterior pituitary extract. Hoff and Potzl[74] obtained contrary results. Oehme and Oehme[75] found the extract to exert its antidiuretic effect after complete degeneration of the renal nerves. In clinical hyperpituitary disease Marx[76] finds that water ingestion causes a long-lasting hydremia, while in hypopituitary disorders anhydremia may result from a simple Volhard water-drinking test.

It has been established by the recent work of Pines[77] and Greving[78] that the pars intermedia and the posterior lobe of the pituitary gland are under central nervous control through fibers originating in the nucleus supraopticus and possibly nucleus paraventricularis. Apparently it is injury to this tract of fibers or their central nuclei which causes the marked polyuria, demonstrated by Camus and Roussy,[79] Ashner[80] and Bailey and Bremer[81] to follow puncture in that region. Houssay and Hug[82] found the polyuria in this experimental form of diabetes insipidus to be primary and not dependent upon polydypsia, glycosuria or increase in blood pressure. Denervation of both kidneys prior to puncture in the region of the hypothalamus, according to them, does not prevent the polyuria. The latter is controlled, however,

by subcutaneous or intranasal administration of posterior pituitary extract. Clinical diabetes insipidus, due to tumor growth or to an inflammatory lesion involving the region of the tuber cinereum or hypothalamus, resembles this experimental form in every way.

Cushing and Goetsch[83] were the first to identify posterior pituitary secretion in the cysternal and ventricular fluids. They did not find it, however, in the spinal subarachnoid spaces. Hoff and Wermer[84] found that either strong emotional stimuli or administration of diuretics leads to an increase in the amount present in the cerebrospinal fluid. Karplus and Peczenik[85] demonstrated a similar response to electrical stimulation of the tuber cinereum. Hoff and Wermer interpret the response to administration of diuretics as a compensatory reaction on the part of the body to prevent excessive loss of water. Cushing[86] has more recently discovered that direct introduction of pitressin into the third ventricle in man causes a typical parasympathetic, or pilocarpin-like, response with flushing of the skin and visible sweating, while intramuscular or subcutaneous injection, of course, produces a typical sympathetic reaction. The spinal anesthetic, avertin, and atropine both prevent the parasympathetic response from intraventricular administration. This newer work on the action of the pituitary secretion and the vegetative centers in the diencephalon serves to emphasize still further the fact that the neuroendocrine mechanism plays a predominating rôle in the regulation of the water metabolism.

The extreme polyuria of experimental or clinical diabetes insipidus has long suggested the elaboration in the body of diuretic hormones which are normally balanced by the antidiuretic pituitary secretion. Bourquin[87] and Olivet[88] have both reported the presence of a strongly diuretic extract from the diencephalon. Bourquin obtained such a diuretic principle from the region of the mammillary bodies, but not elsewhere in the brain, in dogs with experimental diabetes insipidus. She found the same substance in the blood and urine of these dogs but not in normal animals. Trendelenburg,[89] using slightly different technic, failed to confirm these findings. Teel[90] reported finding a markedly diuretic substance in an extract from the anterior lobe of the pituitary body. To my knowledge this has not as yet been confirmed by other workers. The observation of Hann,[91] however, is of special interest in this connection. He demonstrated that polyuria ceased terminally in cases of diabetes insipidus due to lesions of the posterior lobe of the hypophysis, when the lesion gradually encroached upon and destroyed the anterior lobe.

Pick,[42] Glaubach and Molitor,[92] Porges,[93] and Grossman[94] have all reported the presence of a strongly diuretic principle in the liver, administration of which is said by Pick to be effective in certain cases of nephrosis and in uremia from experimental reduction of kidney substance. Ivy[96] has demonstrated that secretin has a mildly diuretic

effect. Although there is no definite proof of such a relationship, it is barely possible that these substances play a special rôle in water diuresis.

Eppinger[97] demonstrated the importance of the thyroid hormone in water metabolism, showing it to have a mildly diuretic action. E. Z. Epstein[98] and others have shown that this diuretic effect of thyroxin is due, not to any direct action on the kidneys, but to its mobilizing fluid from the tissues into the blood. Pituitrin inhibits the diuresis of thyroxin. In myxedema or cretinism, thyroid extract causes removal of stored water and NaCl from the tissues in a specific manner. Ordinary diuretics acting primarily on the kidneys do not remove the excess fluid in such cases. In some types of edema parathyroid extract has been shown by Mason,[99] Meakins,[100] McCann,[101] Reitzel and Stone,[102] and others to exert a diuretic action. We have also seen striking examples of this effect. The observation by Baar[103] of increased water in the brain tissues of subjects with infantile tetany is interesting in this connection. This author considers the increased hydration of the brain tissue to be of primary significance in the symptom complex. Parathormone, of course, is specific in relieving this type of overhydration. Ellis[104] has reported a similar increase in water content of the brain in guanadine tetany, as well as in the tetany of experimental parathyroprevia.

Drabkin[105] and others have demonstrated the tissue hydrating effect of insulin and have pointed out the importance of water in the action of insulin on the carbohydrate metabolism. According to Drabkin, insulin convulsions appear to be more closely related to increased hydration of the brain tissue than to the hypoglycemia *per se*. The retention of fluid which follows administration of insulin in cases of severe diabetes mellitus with dehydration often goes beyond the point of normal rehydration to one of edema formation.[106] Schiff and Choremis[107] showed that dehydration decreases the efficiency of carbohydrate metabolism and insulin action. Whether or not an endocrine factor is involved in the water retention associated with obesity is not known. The circulatory factor is probably sufficient to account for the phenomenon in most instances.

That the internal secretion of the adrenal cortex plays an important rôle in the regulation of the fluid balances of the body is indicated by the recent reports of Swingle[108] and coworkers and by Silvette.[109] The former found that water enters the tissues from the vascular system at an abnormally rapid rate in adrenalectomized animals, causing the blood volume to shrink and the blood pressure to fall progressively to the death level, unless an extract of the gland is administered. Silvette found that adrenalectomized rats excrete less urine and more chlorides than normal animals under the same fasting conditions. A definitely reduced ability to eliminate injected fluids was found in

animals suffering from cortical insufficiency. The muscles and parenchymatous organs of animals with adrenal insufficiency showed a higher water content than normal, while the blood showed concentration, from which the author concludes that the impaired ability of the kidneys to excrete water is extrarenal in origin.

STATE OF HYDRATION AND RESISTANCE TO INFECTION

The relationship of states of hydration to infections, quite apart from that involved in heat loss by vaporization of water during fever, is very important. Barbour[110] and Underhill[111] have shown that the blood tends to become concentrated early in the course of a febrile illness. In fever dilution of the plasma precedes a fall in temperature from the use of antipyretics, according to the work of Barbour. Apparently a similar mobilization of water from the tissues into the blood frequently accompanies the natural termination of fever in the acute infectious diseases. Sandelowsky[112] was the first to study the blood concentration, salt balance and weight changes in patients with pneumonia. In seven of his eleven cases the body weight either increased or remained stationary during the febrile period but fell rapidly after the crisis. The four remaining cases showed a precritical loss of weight. In a study of the total base and chloride metabolism in relation to salt and water retention in infants with primary pneumonia, Wilder and Drake[113] observed a negative base and chloride balance, when the intake of these ions was low, but a markedly positive balance when the intake was high before the crisis. In the former case the base and chloride of the plasma were low and the weight loss was rapid, whereas in the latter, those values were normal or elevated and the weight was increased, often with visible edema. Rapid excretion of the stored water and salt accounted for the post-critical loss in body weight. A direct relationship between the mortality rate and the degree of water retention was suggested by the data. These authors, therefore, advise the use of a known NaCl intake (15 c.c. 0.1 N NaCl solution per pound of body weight in 24 hours) to prevent water retention. Sunderman and Austin[114] confirmed these findings as regards water retention in pneumonia and showed definitely that there was a percentile increase in the water content of the tissues during several precritical days. While the evidence for water shifting due to infection is more spectacular in pneumonia than in most febrile illnesses, the same general reaction appears to be common to all diseases of this class and to serum sickness as well.[115] That water shifting is involved in the related allergic phenomena is indicated by the experimental studies of Rubin and Kellett[116] who found that dehydration has a strongly protective reaction against the harmful effects of anaphylactic or histamine shock. Chronic water-logging of the tissues apparently lowers the resistance to acute infection, as attested by the well-

known increase in susceptibility of so-called hydrolabile infants and of patients with nephrosis and chronic cardiac anasarca. Preliminary experiments now being conducted in our clinic by Doctor Ross Weisiger suggest, so far as they go, that the optimum state of hydration for resistance to acute infection may be one of mild dehydration.

WATER CONTENT AND FUNCTIONAL ACTIVITY OF NERVOUS TISSUE

The possible relationship between the state of hydration of nervous tissue and increased irritability has already been alluded to in our discussion of "water intoxication," tetany and the mechanism of insulin convulsions. From what little evidence is available, it appears to be a rule that the greater the degree of hydration, the more irritable nervous tissue is. Of course, the fact that the various electrolyte equilibria and other factors are often equally important must not be overlooked. It seems probable that the increased ease with which infants and young children have convulsions, as compared with adults, may depend in part upon the significantly greater water content in their brains. Whenever nerve tissue is injured, it imbibes water and becomes more irritable.

Barbour and his coworkers[117] have demonstrated an increase in the water content of the brain produced by withdrawal of morphine from morphine edicted dogs. This increased hydration of the brain tissue is given by them as the cause of the nervous tremors and increased excitability in such subjects. Barbour[118] has shown also that ether anesthesia, as well as morphine narcosis, is accompanied by a decrease in the water content of the brain. The brain edema found at autopsy in cases of nephritic uremia, status epilepticus and eclampsia in pregnant women is well known. The work of Gamble,[119] Fay,[120] the author,[121] and others has demonstrated that a deficit in the body water tends to favor cessation of convulsions in epilepsy, while a positive water balance increases the convulsive tendency. That associated disturbances in the mineral balance of the brain cells may be of importance in this connection is indicated by the more recent experimental studies of the author and his coworkers.[64, 122] Like many of the other problems of water metabolism, however, that concerning the precise relationship of tissue hydration to convulsive phenomena is greatly involved and will undoubtedly require far more extensive scientific investigation for its ultimate solution.

In the present hurried review we have been able merely to sketch the vague outlines of the field of water metabolism in relationship to clinical medicine. Nevertheless, it may suffice to stimulate additional interest in a comparatively neglected phase of practical physiology, which holds unusual promise for the future investigator.

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CHRONIC PEPTIC ULCER IN CHILDHOOD

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ONE usually associates peptic ulcer with adult life and any great deviation from this occurrence stands a very good chance of being overlooked. It is difficult for any doctor with a wide variety of cases to school himself against accepting the law of averages as it applies to the etiology, diagnosis and prognosis of a given disease. Even experience is sometimes fallacious, as a disease may express itself in an atypical form when transplanted in a new environment.

While gastric and duodenal ulcers in children are not common, neither are they so rare that they may be disregarded. It would seem from the literature on the subject that the pathologist has been credited with more familiarity with the disease than his confrere, the internist.

The acute cases may be considered briefly. The majority of cases of acute perforation of peptic ulcer have terminated fatally without any conception of the real cause until the necropsy disclosed the truth. Stern, Perkins, and Nessa[1] report a case of perforation of a gastric ulcer which occurred in a two-day-old infant. X-ray diagnosis was made prior to operation. From this age on, about thirty references to peptic ulcers were found, chiefly of the acute type. We would dispose of the acute type by stating that the etiology is not understood, but assumed to be due to one of several conditions, chief among which are burns and the ingestion of a foreign body. The symptomatology is like that of the acute abdomen of the adult and offers even greater difficulties in recognition of the essential cause. The correct diagnosis has been rarely made, and the mortality must be extremely high. This discussion will be restricted to the chronic ulcer.

Proctor[2] reviewed the literature in 1925 and found nineteen reported cases of chronic peptic ulcer, but in three of these neither x-ray, operation nor autopsy confirmed the diagnosis. In The Mayo Clinic from 1906 to 1924 only two of eight thousand two hundred and sixty cases of peptic ulcer occurred in children. Whether this represents the true ratio between the adult and the juvenile type it is impossible to state. Our search has been fruitless so far as determining the relative frequency of the disease in the several decades of life.

Foshee[3] reports eighteen cases of gastric ulcer in children and adds one of his own. Fourteen cases were successfully operated upon, four died, and one recovered under medical treatment. One can justly inquire whether these figures truly represent the real mortality, when

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it is recalled that successful cases are reported with far more frequency than those that succumb to the disease with or without operation. The careful scrutiny of the reports of a large number of hospitals for children would be the only basis for a rational deduction.

There seems to be little or no available data concerning many features of the etiology, such as the race, habits, climate, food or hereditary factors. When one thinks of the great variety of foods used by children of this country, and the contrast in living conditions, it would seem that if diet enters into the cause of ulcer it should be apparent after a careful survey. The reported cases do not suggest such a relation. In these days of the cafeteria and the delicatessen, it would seem that ulcer would be the logical result of the indiscriminate barrage to which the gastrointestinal tract is subjected, if food plays any part in the etiology of ulcer. In the absence of any known etiology, most writers on this subject believe the cause is the same as in the adult. This seems to be another way of saying we do not know. We can surely eliminate alcohol, tobacco, and financial worries among the causes in children.

The ulcers have about the same anatomical distribution as in the adult, namely, on the lesser curvature near the pylorus and on the anterior wall of the duodenum. This will apply to 90 per cent of the cases. The ulcers go on to perforation or may heal and obstruct the pylorus by the cicatrix. No case of carcinoma which had its origin in a recognized ulcer has been reported in a child.

The symptoms are somewhat vague, except in the cases of perforation, and in those cases they have the symptomatology of peritonitis. If a careful history is obtained it will be noted in the majority of cases that the child has had some dyspepsia over a period of months. Usually the pain has been too mild to attract attention and at other times it has been cramplike. The relation to food and remission of symptoms have not been prominent. It is not unlikely that the appendix has been removed during one of the attacks, but without relief of the dyspepsia. The outstanding symptom, if present, and it is present in 40 per cent of the cases, is the vomiting of blood, or blood in the stools. This one symptom means more than all the others combined and associated with dyspepsia, should be the incentive for as thorough an examination as we would give the older patient. Other symptoms which have been noted are vomiting, hunger pain, epigastric pain, loss of weight, anemia, constipation and underdevelopment. These symptoms are so common to childhood that they lose their diagnostic significance. Children are so prone to vomit and suffer cramps that these symptoms, ordinarily of prime importance in any abdominal complaint in an adult, are generally dismissed with a dose of castor oil and an indictment of the previous meal. Only the most painstaking examina-

tion can elicit the complaints from an intelligent child that the man or woman would disclose with cheerful garrulity.

It is so exceptional that the diagnosis of chronic ulcer is correctly made that one hesitates even to suggest it. One essential is to realize that chronic peptic ulcer in children is possible. With this fact in mind, chronic dyspepsia in a child should certainly excite our suspicions and demand the use of the x-ray. Few roentgenologists are willing to go further in diagnosis of chronic ulcer than to state that an organic lesion is present in the prepyloric region or the duodenum, unless a typical crater is present. Hematemesis or melena, in the absence of a known cause, points strongly to the presence of an ulcer, and with a roentgenogram showing an organic lesion near the pyloris, the diagnosis is almost conclusive.

The treatment offers very much and should be medical primarily, unless confronted with a surgical emergency. Too few cases have been reported in which the medical treatment has been checked before and after with the x-ray. The diagnosis could scarcely be in doubt in some cases that have responded promptly to dietary measures and remained well over a period of years. The Sippey treatment has been generally used. Surgery is necessary in the perforation, the pyloric obstruction, and in the case that does not respond to long and careful medical measures. When an operation is demanded, except for perforation, a plastic operation on the pylorus, such as the Mayo, Judd, or Finney should be the one of choice, and the posterior gastroenterostomy reserved for that type in which the former operations are inappropriate or impossible. We wish to report two cases.

CASE 1.—Miss D. F. of North Carolina, fifteen years old, referred by Dr. William Gerry Morgan, from whose records these notes were made.

Family History.—Parents living and well. Two brothers died of accidents. Other brothers and sisters (four) in good health.

Past History.—She has had the milder diseases of childhood. Since the age of six has had "bowel trouble," and at this age had her first hemorrhage from the bowels. She has never been robust since. Her tonsils were removed a year later, and at the age of thirteen an appendectomy was done.

Present Illness.—Beginning at the age of six, with her first hemorrhage, she has suffered with pain in the region of the gallbladder or pylorus, and constipation has been pronounced. She has been on a diet which contains much roughage, but without relief to either the pain or constipation. There have been intervals of relief from the pain, and then vomiting and pain would return, lasting periods of three weeks approximately. Since February, 1932, she has had less relief and on seven different occasions macroscopic blood has appeared in the stools.

Physical Examination.—Weight 101½ pounds, height 64¼ inches. Skin clear and of good color. Respiratory murmur clear and breezy, no râles, expansion good. Heart sounds were regular, clear, rate 72 per minute—apex beat not displaced. Liver dullness normal. Gallbladder could not be felt and no tenderness elicited.

Abdomen.—Panniculus spare, belly flat, spine prominent, splenic dullness normal. Old well-healed appendiceal scar. Abdominal reflexes exaggerated. Recti of good tone. Only tenderness to be noted is at the site of the appendix scar.

Gastric Analysis.—Free HCl 56, combined acidity 11, total acidity 66.

Blood Examination.—R.B.C. 4,400,000; W.B.C. 7500; Hg 79; 48 polymorphonuclears; 46 lymphocytes; 4 eosinophiles; 1 basophile; 1 large mononuclear. Marked achromia. Coag. time 2½ minutes.

The examination of the urine showed no abnormal constituents and the stool was negative for blood. B.M.R., 12 per cent, 17 per cent, 5 per cent on three different occasions. The x-ray examination is reported as follows:

"The chest is negative. The stomach shows marked reduplication of the mucosa. The rugae are very prominent throughout the entire stomach and the same condition also causes deformity of the duodenal cap. The appearance is that of a baggy redundant mucosa and strongly suggests polyposis in the duodenum. It is noted that at the 24-hour period the stomach is filled with some opaque material, probably some bismuth or other opaque material taken by the patient. The cecum is dilated but is otherwise normal. The entire colon is spastic but shows no other abnormality. There is no evidence of periapical disease of the teeth. Re-examination one week later, of the stomach and duodenum after the administration of belladonna shows the same appearance as at the previous examination. There is marked redundancy of the mucosa throughout the entire stomach and the deformity of the duodenal cap is exactly the same. Diagnosis—Gastric polyposis."

Operation.—On June 3, 1932, the abdomen was explored through an upper right rectus incision. The stomach wall was markedly hypertrophied. An active ulcer, about 1 cm. in diameter was found on the anterior wall of the first portion of the duodenum. It was excised, and a posterior gastroenterostomy was done. The fixation of the duodenum made a pyloroplasty difficult to execute and it was not attempted. No other abnormality was found in the abdomen.

The patient's recovery was without incident and she has remained well.

CASE 2.—M. S., female, seven years old. This patient was seen in consultation with Dr. Robert A. Bier, who kindly furnished me data of which the following is an abstract:

Family History.—Father, Filipino; mother, Greek; patient born in France.

Past History.—Early past history irrelevant except she has been somewhat undernourished and underdeveloped all her life. In January, 1932, she was first seen and a diagnosis of juvenile pulmonary tuberculosis was made. She was seen at infrequent intervals until June 6, when x-ray examination reported lungs essentially clear.

Present Illness.—July 21, 1932, patient reported complaining of pain in the abdomen during the previous two days, following some indiscretion in diet. The physical examination was negative. In November, 1932, patient's mother reported that the child had tarry stools in two successive days. Pain and fever were absent. The physical examination at this time was reported as follows:

The patient is a small swarthy female, seven years of age. Outside her underweight and marked anemic appearance, the physical examination was essentially negative. The examination of the abdomen was carefully made but elicited no positive findings.

The Wassermann was reported negative a few days later.

The stool showed blood in large quantities. The mother stated upon closer questioning that a tarry stool was noted about one year previously, but she failed to mention it until this time. The following day two more bloody stools were reported and patient was admitted to the Children's Hospital and a blood examination made at that time was reported as follows: Hemoglobin, 38 per cent (Newcomer); erythrocytes, 2,550,000; leucocytes, 8,200; lymphocytes, 30; polymorphonuclears, 70; lobulated, 64, band forms, 4, young forms, 2.

Tuberculin test negative.

Urine contained albumin upon the first examination but three days later albumin was absent.

A few days after admission to the hospital the child complained of mild pain in the abdomen.

The x-ray examination of the gastrointestinal tract, made at this time, reads as follows: "The esophagus is normal. There is a constant deformity at the pyloris and at the base of the duodenal cap with approximately 10 per cent six-hour residue. Appearance is that of an ulcerative lesion at the pyloris. Appendix normal. Colon normal throughout."

The patient was placed on a diet of the Sippy type and at last accounts was making excellent progress, without recurrence of blood in the stools. Operation was not indicated, in our opinion.

This presents almost a typical case of duodenal ulcer in a child, and if the bloody stools and x-ray examination could be eliminated from the history, the diagnosis would not be possible. This emphasizes the importance of melena as a symptom and the necessity of x-ray examinations in suspected cases.

COMMENT

That a child may have a chronic peptic ulcer must be an accepted fact, and the few cases reported (excluding those attended with perforation) indicate that a better understanding of the symptomatology is necessary if the disease is to be recognized in a fair percentage of cases before a serious complication discloses the real nature of the disease. There has not come to our notice any extended study of dyspepsia in childhood, having in mind the possibility of peptic ulcer, that included such examinations usually employed in the adult. We are convinced that such an investigation, no doubt beset with many difficulties, would have its own reward in setting up a clinical concept of ulcer in children and permit a better classification of diseases that are obviously mislabelled.

There is hardly a surgeon of wide experience who has not removed an appendix from a child in which the pathology found did not explain the symptoms. The recovery of the patient is his chief source of comfort as he knows only too well that the diagnosis was missed. That his consultants were equally wrong adds a little balm. It is not unlikely that some of these cases are peptic ulcers, as in one case herein reported.

Is it not possible that if the subject of dyspepsia in children were given the same intensive consideration bestowed on many other human ills, a group of symptoms would be found that makes the recognition of the disease possible in its early stages? At the present time no such group of symptoms, no x-ray studies, no pathological set-up is available, based on a large number of cases. The need is apparent and no doubt will be met.

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THE SERUM ALBUMIN AND GLOBULIN OF NEWBORN, PREMATURE AND NORMAL INFANTS

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THE concentration of serum proteins has been studied for years. However, most of the pediatric literature concerns determinations by physical methods (particularly by refractometry) which give large and uncertain errors. Recent work emphasizes the different functions of globulin and albumin. The physical methods for determining the albumin and globulin are even more erroneous than similar methods for estimating the total protein. Although the chemical methods occasionally give false results in the separation of the fractions of serum proteins, a sufficiently true picture can be obtained in this way to warrant an examination of infants' serum. This paper reports the total protein, albumin, and globulin concentrations of newborn, normal infants from the fourth to the eighth month, and premature infants. In addition, a few determinations in pathologic conditions are listed. The data form a standard for evaluating protein concentrations during the first year of life.

LITERATURE

Mello-Leitao[1] reviews the literature on serum proteins in infants estimated by refractometry. This work shows that the serum proteins are lower in young infants than in adults and that the proteins increase gradually during the first eighteen months of life. Marriott[2] and others found the serum protein low in undernutrition and marasmus. Mello-Leitao obtained high values in congenital syphilis.

Webb[3] using the colorimetric method of Wu, which gives slightly high values for albumin, found for young babies the following values: total protein 6.04 per cent, albumin 4.41 per cent, and globulin 1.63 per cent. The rise in the total protein with age was shown to consist of an increase of proportionately more globulin than albumin. Simple undernutrition gave essentially normal values. No striking change with infections was found except in bone tuberculosis, osteomyelitis, and infections accompanied by albuminuria. Infections of the bones were quite regularly accompanied by increase in globulin, while albuminuria was accompanied by decrease in albumin and sometimes by an increase in globulin.

The association of the precipitin reaction with the globulin has led to examination of the effect of infections on this fraction of serum protein. The occurrence of colon bacillus septicemia in calves which receive no colostrum was shown by Smith and Little[4] and Howe[5] to be accompanied by a failure to obtain globulin.

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Normally, calves receive globulin from colostrum. They point out that Ehrlich's immunologic studies indicated that certain animals with thick placentas are born without serologic immune bodies and receive these substances through the colostrum. Other animals, including human beings which have thin placentas, are born with serum globulin and have no disease analogous to the colon bacillus septicemia of calves. Achard, Bariéty and Codounis[6] compared the concentrations of albumin and globulin in eleven normal maternal serums with those of the cord blood of the infants. The albumins were of the same order of magnitude but the globulin was definitely lower in the cord blood.

A number of observers (Starlinger,[7] Rowe[8]) using the physical methods have found slight increases in globulin during the course of infections. Wiener and Wiener[9] found by precipitating the globulin with magnesium sulphate, an increase in globulin in severe infections. Hurwitz and Meyer[10] and Hurwitz and Whipple[11] studied the changes in serum protein by the refractometric method of Robinson in rabbits and dogs. Increase in globulin occurred during the production of active immunity but the rise occurred before immunologic evidence of antibodies could be detected. Since injury to tissues seemed to be a regular accompaniment of procedures leading to increase in globulin, these authors felt that the increase of globulin occurring in infections was most likely associated with disturbances in metabolism rather than development of immunity. Loeper, Ravier, and Lepert[12] found rather striking increases in globulin at the time of the crisis in pneumonia.

Since the present paper includes no cases with albuminuria it is not necessary to consider the striking reduction of serum albumin occurring with marked albuminuria.[13] Attention should be called to the fact that reduction of albumin is the chief factor leading to edema in nephritis and in nutritional disorders. Experimental results indicate that globulins regenerate more rapidly than albumin after depletion of serum proteins by plasmapheresis.[14]

METHODS

The proteins were determined on venous serum of blood taken from the femoral or jugular veins of infants. The determinations were started not later than three hours and usually within an hour of the venipuncture. Nitrogen was determined by Kjeldahl (Peters and Van Slyke[15]) on 1 ml. of serum. In cases where insufficient serum was available nitrogen was determined on 0.2 ml. of serum by the gasometric method of Van Slyke. Albumin was precipitated by the method of Howe[16] using sodium sulphate in the earlier determinations and using K_2HPO_4 plus KH_2PO_4 in the later determinations. While we think the latter method preferable, the two procedures give comparable results. The gasometric determinations check with Kjeldahl determinations. It should be mentioned that the salting out of globulin is not a strictly quantitative procedure and gives occasional false results (Weech[17] and others[18]). When the salting out fails to work as expected, the results are in the direction of low values for albumin. As low albumin was seldom found in this study we feel that the results are reliable.

RESULTS

Since certain analyses were undertaken to establish the variation within fairly homogeneous groups, it does not seem necessary to publish the data in detail. Chart I shows the frequency of distribution of various concentrations. The abscissae represent the concentrations of total protein, albumin, and globulin and the albumin-globulin ratio and the ordinates, the number of observations. The number av indi-

cates the arithmetic average, ± the "probable error" of the average, and σ the standard deviation.

The group of cases labeled "newborn infants" was selected from normal babies in the nursery of the maternity ward. The blood specimens were obtained after the third day of life at a time when weight was increasing or had ceased to fall for two or more days. The group labeled "normal infants" was made up of cases obtained chiefly from the Children's Community Center of New Haven. The ages ranged from one hundred and fifty days to one hundred and eighty days, except for two babies who were aged two hundred and ten days. The latter do not differ significantly from the former. Infections were

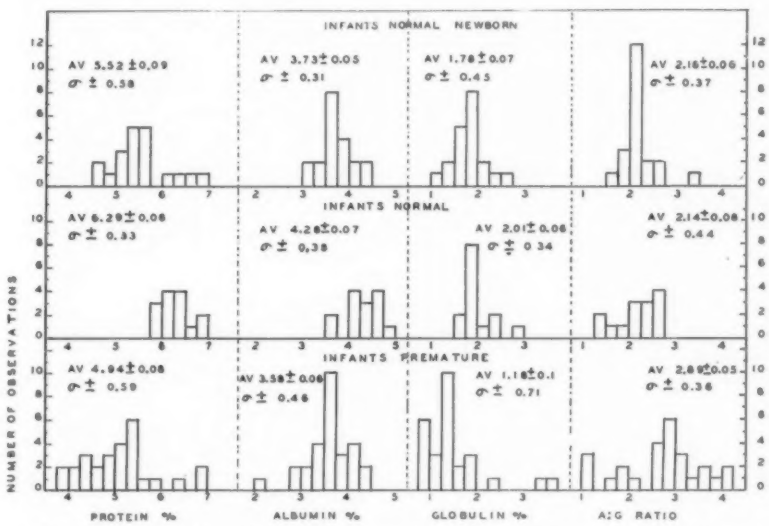

Chart 1.—Distribution of concentrations of serum protein, albumin, and globulin and the A:G ratios. A V give average ± the probable error of the average. σ is the standard deviation.

ruled out in this group by history and physical examination. The group of premature infants was selected from those doing well at the time of the examinations. Since in most cases it did not seem advisable to take blood in the early weeks of life, the samples were obtained after a gain in weight had occurred for two or more weeks. Infections were ruled out in this group as far as possible. The birth weights of the prematures ranged from 1400 to 2500 grams and the ages from six to ninety days. In the premature group, the two analyses with a globulin concentration over 3.0 per cent were considered aberrant (probably due to a failure to obtain proper separation of albumin from globulin) and were not used in computing the averages.

Inspection of the chart reveals that the total protein is widely scattered in each group so that there is considerable overlapping of single determinations of the various groups. The differences between the averages of the various groups ± the "probable error" of the differences are tabulated in Table I. Since a difference which is three times the "probable error" of the difference can only occur through chance sampling in about 5 per cent of the cases, such a difference

TABLE I

DIFFERENCE BETWEEN AVERAGE CONCENTRATION ± "PROBABLE ERROR" OF DIFFERENCE

	PER CENT PROTEIN	PER CENT ALBUMIN	PER CENT GLOBULIN	$\frac{A}{G}$
Normal—Newborn	+0.76 ± 0.11	+0.55 ± 0.09	+0.23 ± 0.09	−0.02 ± 0.10
Newborn—Premature	+0.58 ± 0.12	+0.15 ± 0.08	+0.60 ± 0.12	−0.73 ± 0.08
Normal—Premature	+1.34 ± 0.10	+0.70 ± 0.09	+0.83 ± 0.11	−0.75 ± 0.09

may be regarded as significant. This test of significance confirms the impression given by the chart that the concentration of the total protein is greater in the older normal infants than in the newborn and greater in the latter than in the premature. Although the average albumin of the premature infants is slightly lower than that of the newborns, this difference cannot be regarded as statistically signifi-

TABLE II

POSTMORTEM BLOODS IN FETUSES

WT. GM.	PER CENT PROTEIN	PER CENT ALBUMIN	PER CENT GLOBULIN	$\frac{A}{G}$
650	4.02	2.63	1.39	2.0
780	5.19	4.04	1.15	3.5
850	3.50	1.54	1.96	0.8
1500	5.88	3.65	1.73	2.2
1400	3.58	2.51	1.07	2.3
1200	3.89	1.65	2.24	0.7
1500	4.10	3.13	0.97	3.2
1025	3.76	2.57	1.19	3.1
1900	3.32	2.31	1.01	2.3

cant. However, the albumin of older normal infants is definitely higher than that of the other two groups. The globulin is also higher in the older normal infants than in the other two groups and higher in the newborns than in the prematures.

The use of the albumin-globulin ratio is not altogether satisfactory but is so generally employed that these values were computed. The ratio depends on the accuracy of the determinations. Since globulin is determined by difference, any error in the albumin determination becomes greatly magnified in the albumin-globulin ratio. For this reason conclusions should only be drawn from changes in albumin or globulin concentration. Our data indicate that the proportion of globulin is reduced in premature infants.

Since the finding of low globulin in premature infants might depend on failure of globulin to develop till late in fetal life, several specimens of fetal blood were examined. In these cases for various reasons, labor occurred early but the fetus died late during labor or within one or two hours after birth. The blood was taken immediately after death. The results are given in Table II. We do not wish to draw conclusions concerning the concentration of albumin or globulin during fetal life from these figures, but merely point out that they do not indicate any decrease in the proportion of globulin in the serum of fairly small fetuses.

Since certain infections are known to raise the globulin, a study of the serums of babies with infection should reveal a failure of infants to react in the usual fashion. Table III gives results in various conditions. In the last four cases, the patients were prematurely born.

TABLE III

SERUM PROTEINS IN INFANTS WITH INFECTIONS

CASE NUMBER	AGE DAYS	DIAGNOSIS	DAYS ILL	PROT.	ALB.	GLOB.	$\frac{A}{G}$
1	330	Measles, Pneumonia	14	6.16	3.62	2.52	1.4
2	210	Syphilis	210	7.08	4.08	3.00	1.4
3	250	Scurvy	60?	6.39	3.48	2.91	1.2
4	150	Rickets, Eczema	90?	6.74	3.41	3.33	1.0
5	250	Otitis Media	90	7.75	3.78	3.97	1.0
6	330	Pertussis, Pneumonia	30	6.62	4.10	2.62	1.6
7	65	Undernutrition	?	5.34	3.61	1.73	2.1
8	120	Poliomyelitis	10	5.34	3.05	1.29	1.8
9	210	Mental Deficiency	210	7.46	5.73	1.73	3.3
10	100	Malnutrition, Diarrhea	?	5.74	4.14	1.60	2.6
11	180	Cerebral Palsy, Unexplained Fever	28	6.22	3.95	2.27	1.7
12	270	Rickets, Tetany, Rhinorrhea	30	6.80	5.14	1.66	3.1
13	77	Microcephalus, Otitis Media	14	6.41	4.63	1.78	2.6
14	180	Otitis Media, Convulsions	14	6.91	4.31	2.60	1.7
15	180	Pneumonia	5	5.39	2.92	2.47	2.0
16	60	Syphilis	60	5.72	2.63	3.09	0.9
17	180	Otitis Media, Diarrhea	7	6.32	4.18	2.14	2.0
18	200	Chronic Pneumonia	30	6.57	3.87	2.70	1.4
18	210	Chronic Pneumonia	40	6.95	4.43	2.52	1.8
19	70	Pneumonia	70	6.26	4.33	1.93	2.2
19	90	Recovered	90	6.51	4.27	2.24	1.9
20	330	Otitis Media	10	6.74	4.19	2.55	1.6
21	360	Dermatitis ?	30	6.22	2.56	3.66	0.7
22	?	Neonatal Sepsis	?	6.05	2.99	3.06	1.3
23	120	Diarrhea, Otitis Media	10	7.10	5.48	1.62	3.4
24	80	Diarrhea, Otitis Media	14	5.60	2.28	3.32	0.7
25	25	Diarrhea	7	4.14	2.77	1.37	2.0

We may conclude that single determinations almost certainly represent a deviation from normal when they differ from the average of their group more than two standard deviations. Since these babies are of the age of the group of normal infants, they should be compared

to the average of this group. Applying this criterion six albumins are low: Cases 3, 4, 8, 15, 16, and 21. Case 21 was a peculiar unclassifiable skin disease resembling Leiner's dermatitis exfoliativa, and was the only one manifesting edema. Undernutrition probably played a part in reducing the albumin in the cases of scurvy, eczema, pneumonia, and syphilis. Case 9 (mental deficiency) probably showed a high albumin because of an unsuspected dehydration. The globulin was high in Cases 2, 3, 4, 5, 6, 18, and 21. The most striking elevations are in the patients with syphilis and skin infections.

Since opportunity to study premature infants with infection who are not also dehydrated does not occur often, such cases are few in our series. Cases 24 and 25 suggest that premature infants are apt to develop low albumin with diarrhea and infection. Cases 20 and 24 demonstrate that premature infants can produce a high globulin content in their serums.

DISCUSSION

The average values for adults (Peters and Van Slyke[19]) is: for men, protein 7.00 per cent, albumin 4.44 per cent, globulin 2.58 per cent and A:G ratio 1.72; for women, protein 7.02 per cent, albumin 4.35 per cent, globulin 2.68 per cent and A:G ratio 1.62. Plass and Mathews,[20] Oard and Peters[21] and others have shown that a decrease in serum albumin occurs during pregnancy. Our data indicate that older normal babies have about the same albumin concentration as adult women, but slightly lower globulins. Thus the low proteins of infants is chiefly due to low globulins, though a reduction in albumin corresponding in magnitude to that occurring in pregnant women, is found in newborn infants. In this respect premature infants are like newborn infants, except that their globulin tends to be even lower.

The data on the premature infants showed no relation between the various protein constituents and the age, the birth weight, birth length, and the weight at time of examination. The low albumin may be characteristic of small babies since none of these infants weighed over 2900 grams when the blood samples were taken. Six samples taken during the first thirteen days of life did not differ significantly from the group as a whole. The ages range from six to ninety days, but most of the examinations occurred between the twentieth and fortieth day after birth.

The work of Achard, Bariéty, and Codounis demonstrates that infants are born with about the same concentration of albumin as their mothers, but with definitely lower globulins. This fact suggests that albumin may diffuse across the placenta but apparently globulin behaves somewhat differently. The production of albumin is interfered with in severe undernutrition (Bruckman, D'Esopo and Peters,[22] Frisch, Mendel and Peters,[23] Weech and Ling[24] and others). Our data indicate that albumin concentration is more constant than globulin

concentration. After depletion of serum proteins by plasmapheresis, globulin is regenerated more rapidly than albumin.[14] Globulin apparently increases greatly beyond its usual concentration in response to tissue injury[10] and certain infections.[3] Since babies during the first few months of life have suffered from few infections, these observations suggest that infants may have low concentrations of globulin largely due to absence of the stimuli which lead to globulin production in adults.

SUMMARY

The serum concentration of total protein, albumin, and globulin was determined in 20 newborn infants, 14 normal infants, aged about five months, and 26 premature infants. Similar studies in full-term and premature infants suffering from various diseases were made.

The total protein is decreased in all infants, the decrease being due chiefly to low globulin. The diminution in globulin is greatest in premature infants.

Postmortem serum of small fetuses shows essentially the same albumin-globulin ratio as that of full-term infants.

Both premature and normal infants may show an increase in globulin during infection.

It is suggested that the low globulin in infants may indicate the lack of the usual stimuli that give rise to globulin production in adults.

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MANAGEMENT BY MECHANICAL RESPIRATOR OF POSTDIPHTHERITIC RESPIRATORY PARALYSIS

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THE clinical similarity of respiratory failure in late diphtheria and in certain forms of poliomyelitis is apparent to physicians familiar with the two diseases. Wilson[1] has emphasized that poliomyelitis can prevent efficient respiration through direct paralysis of the primary respiratory muscles, through interference with respiration in patients with pharyngeal paralysis in whom inspiration is continually interrupted by unswallowed secretions collecting around the glottis, and finally through a disturbance of the nerve centers in the medulla controlling respiration. Respiratory difficulty in any patient ill with poliomyelitis may be due to a single one of these factors or to a combination of two or more.

The striking difference between respiratory difficulty in poliomyelitis and in late diphtheria is that in infantile paralysis the cause is commonly of central origin, while in diphtheria the difficulty is chiefly concerned with paralysis of the diaphragm and of the intercostal muscles. In both conditions the factor of accumulated secretions following paralysis of the muscles of the pharynx is often important. The careful observations of Wilson have demonstrated that in poliomyelitis the response to management with the Drinker[2] respirator is much more favorable when the lesion is related to the cervical and dorsal cord, with resultant paralysis of the intercostal muscles and of the diaphragm, than when the involvement is primarily bulbar. Our own experience has been the same, and logically led to consideration of this method in the management of late respiratory paralysis in diphtheria.

Since 1927, 5057 cases of diphtheria have been admitted to the wards of the Herman Kiefer Hospital, Detroit. The number of deaths was 632, of which an appreciable number, eighty-seven, were due to the toxic effects of the infection and occurred within the first few days. Circulatory failure was by far the commonest cause of death, being responsible for no less than 415 fatalities. Among patients with the laryngeal form of diphtheria the commonest contributing cause of death was pneumonia, ninety-six cases, with suffocation from obstruction essentially uncommon. Septicemia, generalized suppurative peritonitis, nephritis, empyema thoracis and activated pulmonary tuberculosis were rare causes. Fatality in thirteen instances was due to respiratory insufficiency after paralysis,

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or about 2 per cent of all deaths. The condition is not frequent but when it does occur is of serious moment, in that of twenty-one patients with diaphragmatic and intercostal paralysis thirteen died, a case fatality of 61.9 per cent.

Paralysis of respiratory function in diphtheria is as a rule a late development. The condition is almost completely limited to patients with an original massive infection of the throat, where the membrane involves not only the fauces but extends into the nasopharyngeal vault and generally involves the palate and the uvula as well. The first paralysis to develop is ordinarily related to inhibition of function of the palate, and would seem to depend largely upon local absorption of toxins. It usually appears on the eighth to fourteenth day after onset. The paralysis next most commonly observed involves the muscles of the eye. At about this same time, the third week, a paralysis of the muscles of the larynx and of the pharynx may occur. By the fourth week the muscles of the extremities are likely to be involved, and not uncommonly sensory disturbances are present, indicated by numbness, prickling and hyperesthesia of the extremities. Respiratory paralysis rarely develops other than in the wake of such a progression of paralyses.

In this group of patients the earliest onset of respiratory paralysis was on the twenty-seventh day, the latest on the fifty-sixth. The course of events in overwhelming faucial diphtheria is a severe toxemia lasting four to five days, followed almost invariably by severe circulatory disturbance on the eighth to sixteenth days. In those surviving this hazard paralysis of the muscles of respiration may be anticipated about the sixth week. The time of this reaction is so constant that trouble is looked for at about the thirty-fifth day in the hospital, which corresponds to about the fortieth day of the disease. Our experience in the onset of respiratory paralysis is illustrated in Table I.

Since paralysis of respiratory function occurs only in late convalescence, all deaths from diphtheria have been reviewed in regard to the day of the disease on which they occurred. Of the 632, only twenty-nine were after the twenty-first day. Of these, thirteen were due to paralysis of the muscles of respiration, ten to circulatory failure and six were attributed to bronchopneumonia. Postdiphtheritic paralysis is thus the most common cause of death during convalescence.

TABLE I

DAY OF ONSET OF POSTDIPHTHERITIC RESPIRATORY PARALYSIS

DAY OF ONSET	CASES
21 – 27	1
28 – 34	3
35 – 41	11
42 – 48	5
49 – 55	0
56 – 62	1

Drinker[2] in 1929 reported a mechanical apparatus for maintaining prolonged artificial respiration and gave a description of a fatal case of poliomyelitis treated by the method. Later[3] he presented an analysis of additional cases, suggested the use of the apparatus in the orthopedic treatment of intercostal paralysis, and reported on its use in seventeen cases of gas poisoning, eight of alcoholic coma, five of drug poisoning, and one of drowning. Jackson[4] has described the development of mechanical methods for prolonged respiration. Murphy[5] and others reported a modification of the original Drinker apparatus designed for small children and infants, with an appliance for the administration of oxygen and carbon dioxide in the treatment of asphyxia of the newborn. Murphy, with C. K. Drinker and Philip Drinker,[6] emphasized that respiratory paralysis in the presence of an exudative process in the lungs is likely to make but little progress when managed by the respirator. Reports on the method in poliomyelitis complete the literature.[7] To these indications may now be added another, the application of the method to postdiphtheritic respiratory paralysis.

CASE 1.—Elizabeth K., aged eight years, became ill on December 1, 1931, with sore throat, fever, and headache. The next day the glands of the neck were swollen, she vomited twice and complained of constipation. A well-marked discharge from both nasal passages was present on the third day and the swelling of the neck was exaggerated. She was not seen by a physician until late on the fourth day. He administered 10,000 units of antitoxin and sent the child to the hospital.

The temperature was then 102.4° F., the pulse rate was 120 and the respiratory rate 32. General physical examination indicated a child critically ill. There was a mucopurulent discharge from both nares. The neck was so swollen, because of enlargement of the cervical lymph nodes and the adjacent tissues, as to produce a rounded effect almost obliterating all markings and suggesting the possibility of parotitis. The tongue was markedly coated. The tonsils were so enlarged and swollen that they essentially met in the midline of the throat. A thick diphtheritic membrane covered the entire surfaces of both tonsils, all visible portions of the pharynx, the uvula and the soft palate. Both lung fields were clear. The heart borders were within normal limits. No murmurs were heard. The cardiac sounds were well preserved and the rhythm regular. The child was poorly nourished and pale. Sixty thousand units of diphtheria antitoxin were administered on the evening that the child came to the hospital, and an additional 40,000 units the following morning. On the sixth day of illness, the patient was clinically much worse, and the blood pressure was at the extremely low level of 72/48. The cardiac tones were softer and the heart rate more rapid.

On the fourteenth day the blood pressure dropped sharply to a level which long experience has shown to be compatible usually with no other than a fatal prognosis the systolic pressure being 54 and the diastolic indeterminate. A marked gallop rhythm was present. For the next several days the child was listless, took nourishment and fluids poorly and barely seemed to live from day to day. Palatal paralysis was first noted on the twenty-first day and shortly thereafter paralysis of the muscles of the pharynx, accompanied by the collection of much mucus in the throat because of inability to swallow. Repeated aspiration was performed with a mechanical suction apparatus. On the twenty-fourth day the patient complained of blurring of vision, and within the next two or three days, of general hyperesthesia, particularly numbness and tingling of the extremities. By the thirty-seventh day the

paralysis of the throat had become so extensive as to necessitate feeding by nasal catheter. The circulatory condition was somewhat improved. Throughout the forty-second day, the patient was fairly quiet, but in the early evening became restless and cyanotic from insufficient oxygenation. At 10:30 P.M. the respiratory effort was of such degree that the patient could not be restrained. She continually tossed about and attempted to sit up. Paralysis of the intercostal muscles, which had been first noted three days previously, was at this time so extreme that breathing was almost entirely abdominal. It was felt that exitus was imminent unless aid to respiration could be accomplished. During the course of transfer from her room to the mechanical respirator the child's struggle for air ceased, and there was a gurgling shallow type of breathing indicative of complete exhaustion.

The child evidenced a remarkable change shortly after being placed in the respirator. Within an hour all restlessness had disappeared and she slept comfortably the remainder of the night. The color of the lips and nail beds improved. During the early hours of treatment a pressure of 18 to 20 mm. was used, but the next morning this was reduced to 8 mm. with equally good effect. The following day the patient slept a goodly portion of the day although the machine was continuously in motion. Mucus continued to collect in the throat and was a troublesome factor which demanded repeated use of the aspirating apparatus. The following three or four days were uneventful. On the fifth day the child was out of the respirator twice, for periods of six and ten minutes, during which time respiration was fairly regular, but rapid and somewhat shallow, with movements of the chest exaggerated. After seven days the respirator was no longer required except for periods of exercise. Active respiration was much improved, although the accumulation of mucus in the throat continued a matter of concern. Convalescence was progressive, so that by the seventy-eighth day she was able to be up for the first time and on the eighty-fourth day was discharged from the hospital recovered.

CASE 2.—John W., aged eighteen years, became ill on April 3, 1932, with sore throat and fever of undetermined degree. The next day he complained of chilliness, of abdominal pain and vomited several times. Headache became a pronounced symptom. Swelling of the glands of the neck was first noticed on April 4. During the next two days his illness progressively became of greater moment although he was not seen by a physician until April 7, the fifth day of his illness.

The patient was admitted to the hospital in a critical clinical condition. The fever was 101.6° F., the pulse rate was 88 and the respiratory rate 26. The lips and nail beds were deeply cyanosed. The patient was rational, cooperative, but markedly toxic. The swelling of the neck was not limited to the lymph nodes but involved the tissues about the glands, to give a periadenitis and edema of extreme degree. A gray-white membrane covered both tonsils, extended upward to involve the nasopharynx and forward to completely cover the uvula, the entire soft palate and even part of the hard palate. The distribution of diphtheritic membrane and the severity of the general reaction were about as severe as may be seen in malignant diphtheria. The heart rate was slow but regular. The heart tones were ill defined and muscular. No murmurs were heard.

Antitoxin in the amount of 80,000 units was administered immediately, with an additional 40,000 units the following day. The patient's condition was extremely precarious during the early days in the hospital, subsequently slowly improved, and the mucous membranes of the pharynx were first entirely free from membrane on the eighth hospital day. The blood pressure which at the time of admission was 100 mm. Hg systolic and 70 diastolic, dropped at this time to 82/50 and the heart tones were only of fair quality. On the fifteenth day the patient was very pale and the pulse rate had dropped to 52. There was every clinical evidence of myocarditis

with impending circulatory failure of diphtheria, and complaints of nausea and epigastric pain. The following day a gallop rhythm was well defined. The blood pressure was 75/40. The liver was tender and palpable. Palatal paralysis was noted. On the eighteenth day the quality of the heart sounds was somewhat improved, also the rhythm, and the blood pressure was slightly higher. Dating from that time there was well-marked improvement, so that by the twenty-fifth day the pulse rate was 80 and the blood pressure was 96/66. For the first time, however, he complained of difficulty in swallowing and this was accompanied by an irritative cough.

No distinct advance occurred in the paralysis of the muscles of the pharynx until the fortieth day, when the voice developed a marked nasal quality and the paralysis became so well defined that he had emesis of food through the mouth and nose. The quality of the pulse was not as satisfactory. He spent a restless night. Because of repeated emesis, nasal feeding was instituted. On the forty-first day the respirations were irregular and somewhat shallow, although the pulse was stronger. The patient slept a great deal. He complained of blurred vision. In the course of the early afternoon respiratory effort became pronounced and at 4:45 he was placed in the Drinker respirator, cyanosis being then very definite and the respirations so labored as to be alarming. The pulse rate was 140, and the temperature had increased to 101° F. The paralysis of respiration was distinctly of the intercostal muscles, in that although the rate of respiration was rapid there was little movement of the chest. It was believed that bronchopneumonia was also present.

The pressure of the machine was maintained at 18 to 22 mm. and the rate at 16 and later 32. At no time could the patient accommodate respiratory effort to the rhythm of the machine. He progressively became worse and death occurred at 10:05 P.M., essentially five hours later.

DISCUSSION

The clinical similarity between postdiphtheritic respiratory paralysis and that form of poliomyelitic paralysis reacting most favorably to management with the Drinker respirator indicated the probable value of the method in diphtheria. Our experience would suggest another worth-while use of the method in the field of communicable disease.

In criticism of the conduct of these two cases, we feel that the observation of Wilson applies pertinently here as in poliomyelitis, in that both patients might well have been given earlier advantage of the method. The patient who recovered was placed in the machine within minutes of an expected exitus, and the one whose illness terminated fatally might well have received material benefit by its use at least three days earlier. Our experience with this method in poliomyelitis had been discouraging, to such an extent that we hesitated to make use of it in diphtheria unless no other measure was possible. With the earlier types of apparatus it was difficult to provide ordinary symptomatic and hygienic care. This is not a criticism of the more recent models of the respirator.

If artificial respiration by this method is started at the first sign of difficulty it is believed that a greater proportion of recoveries will be noted among patients with postdiphtheritic paralysis than with any other of the conditions which may be treated by this method.

CONCLUSIONS

The use of the Drinker apparatus for long-continued artificial respiration forms a worth-while addition to present methods of management in postdiphtheritic respiratory paralysis. Two case reports describe one recovery and one death. The early use of the method should conduce to fewer deaths from this uncommon but serious complication of diphtheria.

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NEUROCUTANEOUS SYNDROMES IN CHILDHOOD

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IN THE process of formation of the human embryo from the primitive layers of the blastoderm, structural differentiation may proceed normally to final configuration, or it may deviate from the regular trend of folding with the production of anomalous states. The degree of structural defect will depend in turn upon the stage at which the adverse influences begin to operate. The ensuing anomalies may be such as to cause no disability to the future individual or they may be so marked as to be incompatible with life. They may exhibit, furthermore, a definite tendency to affect predominantly some one of the three layers of the developing blastoderm.

There are three unusual congenital disorders which show marked similarity in their clinical and pathologic manifestations and which involve electively organs having their common origin in the ectoblast, namely, the nervous system, eyeball, retina, and skin. These disorders are von Recklinghausen's neurofibromatosis, Bourneville's tuberous sclerosis, and angiomatosis of the brain associated with vascular nevi in the region of the distribution of the trigeminal nerve. All three conditions have been grouped in the general category of neurocutaneous syndromes. Recently, Yakovlev and Guthrie[1] have proposed that the disorders be classified under the heading of congenital ectodermoses.

Although all three syndromes show central manifestations which are characteristic of each disorder, they are by no means mutually exclusive. They present signs and symptoms which overlap to a considerable extent with an impressive range of variability due to the interplay of factors permitting many combinations of developmental defects. Of especial clinical interest is the occurrence of cutaneous anomalies which are indicative of associated maldevelopments in deeper seated, embryologically related structures, such as the central and peripheral nervous systems. Also of importance is the frequent association of the three congenital disorders with mental defect and epilepsy.

VON RECKLINGHAUSEN'S NEUROFIBROMATOSIS

In 1882, von Recklinghausen[2] published his well-known monograph on neurofibromatosis. The treatise dealt solely with the relationship

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of the peripheral nerves to the subcutaneous nodules and the tumors of the skin. Since then, researches on the problem have tended to broaden that restricted point of view, the disorder being regarded now as a generalized disease involving primarily nervous tissue in any part of the body with secondary changes in other organs. Thus Ewing[3] states that the tumors in cases of neurofibromatosis may occur in the jejunum, ileum, colon, bladder, vagina, pleural cavity, along the intercostal and lumbar nerves, the intervertebral ganglia, the terminal filaments of the sympathetic nerves, as well as in the suprarenal glands. Penfield and Young[4] have emphasized the bizarre and varied clinical manifestations of neurofibromatosis and have called attention to the disclosures at necropsy of large numbers of unsuspected lesions involving both the peripheral and central nervous systems and the meninges.

According to Prieser and Davenport,[5] von Recklinghausen's neurofibromatosis is a disorder showing strong hereditary tendencies. It may recur without a break for generations and may sometimes be familial. The investigators found that in families who were disposed to the disease and in whom there were two or more children, 43.5 per cent of the offspring showed some form of neurofibromatosis. There was a tendency, furthermore, for the growths to affect the same parts of the body in certain families. A careful survey of the literature revealed the occurrence of feeblemindedness in 7.8 per cent of 243 cases.

Clinically, as Yakovlev and Guthrie[1] have stated, neurofibromatosis may assume either a stationary form, a subacute form which is characterized by periods of exacerbation and remission in tumor growth, an acute form showing rapid and generalized development of neurofibromas, or a malignant form undergoing sarcomatous degeneration and giving rise to metastases. There may occur polypoid tumors of the skin, subcutaneous nodular tumors of the peripheral nerve trunks, brownish pigmentation of the skin, and changes in the skeletal system. Epilepsy and mental defect are often present, as well as faulty development of other organs of the body.

The tumors of the skin may occur on any portion of the body, but they are more abundant at the cephalic and caudal ends, and on the dorsal rather than on the ventral aspects of the trunk. They tend to decrease in frequency from the trunk to the distal ends of the extremities, being found seldom on the hands and feet. The cutaneous tumors vary greatly in size and are either polypoid or pedunculated in form. They are soft and usually painless. The subcutaneous nodules or multiple neurofibromas develop along the course of the peripheral nerve trunks, involving most commonly the median, ulnar, and internal cutaneous nerves of the arm and the femoral and sciatic nerves of the legs.[6] The cranial and spinal nerves are also affected, as well as the

spinal roots and the cauda equina. Plexiforme neuromas are quite similar to the multiple neuromas, the main difference lying in the fact that only a small group of nerves is affected, the lesions being more circumscribed. At times, the involvement may be so great that considerable enlargement of the extremities occurs, the condition then being known as elephantiasis neuromatosa (pachydermatocele). Pigmented nevi are commonly present as associated lesions of the skin, and occasionally "port-wine" nevi and the so-called anemic nevi of Vorner.[1] It should be stated that according to Antoni,[7] the tumors of von Recklinghausen's neurofibromatosis are made up characteristically either of apolar tissue (type B) showing no palisading of nuclei or polarization of cells, or, at times, of tissue of the A type, the true perineural fibroblastomas which are of neoplastic nature and composed of fibroblasts displaying both palisading of nuclei and polarization of cells.

In cases of neurofibromatosis, the pigmented eruption of the body, or "café au lait" spots, has always attracted attention. It is usually found scattered irregularly over the body. Its relation to the problem of the origin and formation of skin pigmentation is of particular interest. Block[8] believes that there are two types of skin pigment cells, the melanoblasts, comprising those cells which are capable of forming pigment, and the melanophores or chromatophores, consisting of those cells which cannot elaborate their own pigment but which obtain it from other sources. The human skin contains pigment in its ectodermal and mesodermal parts. The ectodermal pigment cells of the skin, as well as of the mucous membranes, are melanoblasts of ectodermal origin and are found in the epidermis, especially in the basal cells, the hair matrix and in the cells of pigmented nevi. The mesodermal part of the skin, the corium, contains two different kinds of pigment cells. The one type, melanophores, which have phagocytized pigment, is found in the papillae and in the deeper layers, whereas the other type, mesodermal melanoblasts which have elaborated their own pigment, is found in the cutis. Moehlig[9] states that both the posterior portion of the pituitary gland and the suprarenal cortex are concerned with pigment formation, the latter reflecting or mirroring the state of the former. Posterior pituitary lobe extract is a melanophore stimulant and affects particularly mesodermal tissue. The pigmentary changes occurring in von Recklinghausen's neurofibromatosis have been attributed to a disordered state of the adrenal glands. Many cases have been reported in the literature, such as those by Levin[10] and by Tucker,[11] which seem to show a relationship between certain endocrine dysfunctions and neurofibromatosis. The latter author states that from the pituitary standpoint the characteristics are chiefly acromegalic in type, whereas the suprarenal manifestations are pigmentary disturbances, lowered blood pressure, and hypotrichosis.

The true character of the osseous lesions in neurofibromatosis was first described by Brooks and Lehman[12] who found the following types of bone changes which were considered characteristic of the disease: scoliosis, abnormalities of growth, irregularity of the shafts of the long bones, and subperiosteal bone cysts. The irregularity of the shafts of the long bones varied from slight change in outline of the periosteal and cortical structures to large tumors projecting from the surface of the bone or embedded as cyst-like cavities in the structure of the bone. Microscopically, the central portion of the tumor was found to consist of tissue similar to that of the cutaneous lesions, as well as of some newly forming bone. The investigators were of the opinion that the changes were induced by the development of neurofibromas along the nerve filaments in the periosteum, thereby setting up a certain amount of reaction and causing bone destruction and regeneration. Lehman[13] has attempted to classify the various osseous lesions, defining them as manifestations of the complicated disorder of neurofibromatosis and comparing them to its skin and visceral expressions. Recently, Weber,[14] in an article dealing with periosteal neurofibromatosis, also expressed the opinion that in certain cases of von Recklinghausen's disease bony thickenings occur which are due to involvement of the periosteum.

It should be borne in mind, however, that von Recklinghausen's neurofibromatosis is not seen always in its complete clinical form. As Goodhart[15] has stated: "Aside from typical forms of neurofibromatosis, there are also incomplete or abortive forms in which only one of the cardinal symptoms is present, either pigmentation or fibroma, which may be not infrequently combined with mental defects or skeletal anomalies." Many years ago, Weber[16] called attention to the fact that cases occur in which pigmentation of the skin is manifest long before the appearance of neurofibromas of the nerve trunks or tumors of the skin, citing many case records to bear out his contention.

The following case reports illustrate the above statements.

CASE 1.—J. E., male, white, was born at full term on October 8, 1922. The second stage of labor was prolonged and was terminated by the application of forceps. Marked ecchymoses and swelling were present about the infant's eyes. Respiration was spontaneous; there were no convulsions. The birth weight was 10½ pounds (4.76 kg.). The mother, a primipara, was thirty-one years of age and had been married eleven years before giving birth to this boy, her only child. Throughout pregnancy she had maintained good health. There were no previous miscarriages. The father, thirty-eight years of age, was normal physically. The family history was essentially negative.

The infant was fed artificially and manifested an excellent rate of growth, weighing 25 pounds (11.4 kg.) at the end of the first year of life. Development was also normal. Of importance, in the light of future developments, is the fact that shortly after the birth of the infant, the mother noticed a few scattered areas of brownish pigmentation on his body. However, little attention was paid to the eruption at this time. It should be stated here that the pigmentation became more evident sub-

sequently, new areas appearing on the trunk, face, and extremities, each lesion growing in size and deepening in hue. Aside from an attack of whooping cough when he was three years of age, and a retropharyngeal abscess at three and one-half years of age, the boy enjoyed apparent good health up to about five and one-half years.

At this time, he was seized suddenly at night by an attack of projectile vomiting which was followed shortly by a series of convulsions lasting about twelve hours. The temperature was high. He was taken to one of the city hospitals where he was observed for a period of three weeks, no definite diagnosis being made. Following this primary acute attack, the boy became subject to the frequent occurrence of convulsions, both minor and major in severity, some being of but brief duration whereas others lasted from ten to fifteen minutes. For the most part they took place at night while the boy was asleep. They were preceded invariably by sharp piercing cries, pallor and cyanosis, and were followed by clonic contractions of the entire body and a period of unconsciousness. At no time was there frothing at the mouth, biting of the tongue, or loss of sphincteric control. Vomiting did not occur always. Other episodes consisted merely of a trembling of the entire body and momentary loss of consciousness. The attacks occurred irregularly, sometimes taking place daily, whereas at other times an interval of a few weeks elapsed between attacks.

At six and one-half years of age, the boy entered public school, where it was noticed that he had poor eyesight. He was placed, therefore, in the sight conservation class. He was then referred to the Neurologic Institute for examination. It was noted by roentgenograms that the skull showed a tendency toward early union of the sagittal suture but that this had not yet produced demonstrable change in the outline of the skull. The sella turcica appeared to be normal and secondary dentition was progressing favorably. The blood gave a negative reaction both to the Wassermann and Kahn precipitation tests. The von Pirquet test was negative and the basal metabolism was recorded as being minus 3. Of interest is the fact that psychometric tests were performed at this time, with an intelligence quotient of 102 on the Terman scale.

As far as the general behavior of the boy was concerned, he was well-mannered and obedient, amenable to discipline, and never assaultive. His personal habits were good. In school, he associated well with his classmates and showed slow but definite progress in class work, despite frequent periods of absence. Meanwhile, it was noticed by the mother that the pigmented areas on the face and body of the boy, were increasing in number and in size and were becoming deeper tan in color. It was also observed that the was developing a hard tumor on the right side of the nose, directly beneath the inner portion of the right eye. The boy was then referred for admission to the Beth Israel Hospital.

He was now eight years of age, weighed 70 pounds (31.8 kg.) and was 55 inches (139.7 cm.) in height. His head measured 21¾ inches (55 cm.) in circumference, his chest 26½ inches (65.5 cm.), and his abdomen 25½ inches (64.8 cm.) He was fairly well developed and of fair nutrition. The musculature was flabby and the posture poor. He was restless and inattentive. He appeared to be dazed and disoriented; his responses showed a markedly delayed reaction time. Over the entire trunk, face, and extremities, but mainly over the covered parts of the skin, there was seen a generalized, haphazardly arranged, irregularly oval-shaped, pigmented macular eruption, the lesions varying in size from that of a pinhead to 4 or 5 centimeters in longest diameter. (Fig. 1.) Their color ranged from pale tan to light brown. They were equally numerous both on the dorsal and ventral aspects of the trunk and extremities. Directly above and to the outer side of the right nipple there was seen a deeply pigmented nevus. The skin, which was moist and coarse, had a peculiar pale yellowish hue. There was a normal growth of lanugo hair. At this time, no tumor masses were palpable in or beneath the skin.

The head was long and narrow and appeared to be too large for the rest of the body. The upper and lower jaws were prominent and the upper middle incisor teeth protruded forward markedly. The general features were gross and coarse and suggested a disturbance of the pituitary gland. It should be noted, in this connection, that the fingers of the hands were long, broad, and spatulate at the tips. The scalp was covered by coarse, straight, medium brown hair; the eyebrows and eyelashes were normal. The nose was broad both at the base and at the bridge. To the right side there was a bony hard swelling apparently intimately connected with the nasal bone. The overlying skin was freely movable. The palpebral fissures were equal; there was about a 25 degree convergent strabismus of the left eye.

Fig. 1.—Showing the irregularly scattered, oval-shaped, pigmented eruption of the body. Note also the bony tumor on the right side of the nose and the internal strabismus of the left eye.

The right pupil was greater than the left; both reacted normally to light and accommodation. The acuity of vision was 20/100 for the right eye and 20/200 for the left; there was a bilateral myopic astigmatism. The fundi showed a primary optic atrophy. Attempts to estimate the fields of vision either by confrontation or by perimetry were unsuccessful. The ears were normal. The lips were thickened, the vermilion borders being fairly well defined. The upper incisor teeth were larger than normal and protruded forward markedly. The enamel of the permanent teeth was fair. The deciduous teeth showed well-advanced caries. All the teeth were poorly spaced; the occlusion was bad. The mucous membranes of the mouth were of good color. The tongue, throat, and pharynx were normal. There was no lymphadenopathy.

The thorax was symmetrical and the nipples were normal. The lungs and heart were normal. The abdomen was soft; no organs or masses were palpable. The genitals were normal in appearance and the testicles fully descended. With the exception of the broad, flat hands, as has been mentioned before, the extremities were normal, as were the nails of the fingers and toes. Both the superficial and deep reflexes were equal and active; no pathologic reflexes were elicited. The skin was hyperesthetic over all areas.

Laboratory procedures showed that the urine and the blood were normal. The latter gave a negative reaction to the Wassermann test. Glucose tolerance tests were performed, but gave no conclusive information. The spinal fluid showed negative reactions to both the Wassermann and colloidal gold tests. A basal metabolism was attempted under conditions not truly basal and showed a rate of plus 18.

Fig. 2.—Atrophy of the bones of the hands involving the epiphyses and diaphyses, but being more marked at the epiphyseal ends. Note beginning cyst formation in head of first metacarpal bone of left hand.

Roentgenography of the skull revealed that the cranial cavity was somewhat large, particularly in the postauricular portion. The bones of the cranium were of normal thickness; there were no areas of bone destruction or sclerosis and the sutures were not separated. The sella turcica was normal and the air sinuses were well developed. In the right infraorbital region, in the neighborhood of the superior maxilla, there was seen a bony mass which showed normal bone markings and which appeared to be a part of the ethmoidal cells. This mass was evidently that seen externally to the right side of the boy's nose. Encephalography failed to show any definite pathologic condition of the brain. Roentgenograms of the bones of the hands revealed atrophic changes involving the carpal and metacarpal bones, as well as those of the phalanges. (Fig. 2.) The atrophy was very distinctive and involved the epiphyses and the diaphyses, but was most marked at the epiphyseal ends. In the head of the first metacarpal bone of the left hand, there was seen coalescence of several lamellae

which showed changes resembling beginning cyst formation. Similar changes were found to be present in the bones of the metatarsal phalanges, as well as in the bones of the shoulder and hip joints. Films of the chest revealed nothing unusual.

After a prolonged period of observation in the hospital, during which time the boy had but one mild attack of convulsions, he was discharged. Since then, for the past year, the convulsive seizures have occurred frequently, being both of minor and major severity. Whereas previously they took place about once a week, of late they have happened almost daily. Throughout all this time, his general behavior has been fair. However, he has been showing signs of progressive mental and physical deterioration. Mentally, he is unable to grasp new situations easily, his reaction time has increased considerably, and he appears dazed and inattentive. He is unable to concentrate on even the simplest problem and his answers to questions are irrelevant. He seems also to have reached the limit of his learning capacity.

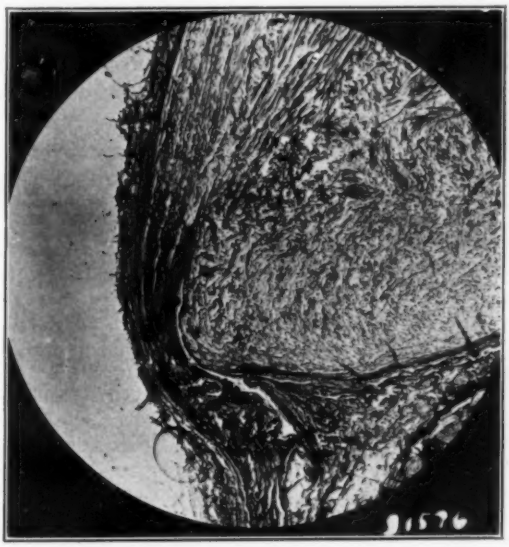


Fig. 3.—Photomicrograph of section of subcutaneous nodule showing nerve trunk and tumor.

Physically, he has shown a slow but steady loss in weight. Transient pathologic reflexes appear from time to time. He walks shakily, swaying from side to side, and shows a general lack of motor coordination.

At a recent follow-up examination, it was noted that several small subcutaneous nodules had developed bilaterally along the course of the superficial branches of the ulnar nerves. In addition, a few had appeared in the occipital areas of the scalp. The boy was then readmitted to the hospital and a biopsy was performed, two of the subcutaneous tumor masses being removed. Grossly the specimens consisted of spindle-shaped swellings having smooth, shiny, gray surfaces and were firm and elastic in texture. The microscopic report confirmed the clinical diagnosis of von Recklinghausen's neurofibromatosis. "The spindle-shaped swellings consist of a highly edematous network of fibers. The fibers are coarser in the center, thinner at the periphery. The edema is very marked at the periphery. The fibers are continuous with fibers from the nerve which are stretched over the node. How far these fibers belong to the nerve proper, how far to the endoneurium, cannot be said with cer-

tainty. The same doubtful behavior is evidenced in the van Gieson stain, where the thicker fibers become intensely red, while the thinner ones, which are continuous with them, are definitely yellow. There is a very fine network of yellow fibers through which nuclei are spread in irregular fashion. Most of the nuclei are ovoid or spindle-shaped. Occasionally, larger, faintly staining plasmatic bodies are seen around the nucleus. In the nonthickened portions of the nerve at the end of the specimen, the endoneurium appears much thickened. On the cross-section, however, the medullary sheath and axis cylinders appear normal, as far as can be judged in this preparation." (Fig. 3.)

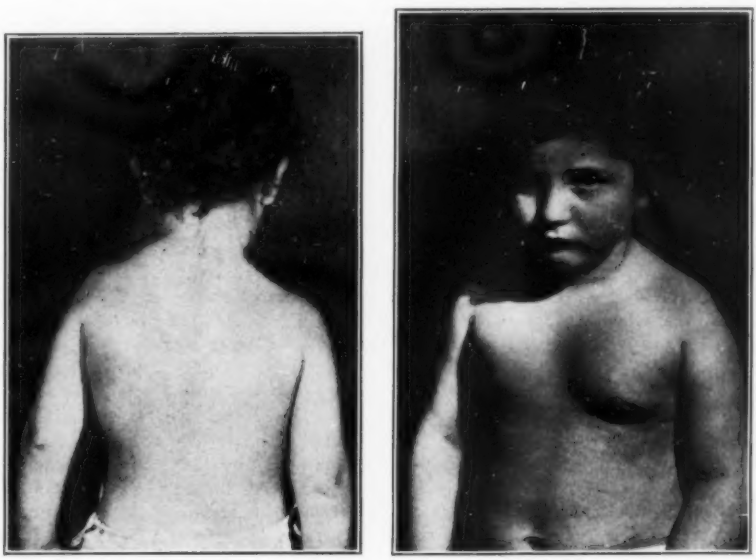
Comment.—In recapitulation, Case 1 is one of neurofibromatosis in a young boy, nine years of age, showing clearly the systemic nature of the disorder. The boy presented pigmented lesions of the skin, subcutaneous peripheral nodules, and definite bony changes. In addition, there were signs of involvement of the central nervous system, as was manifested by epilepsy, signs of progressive mental deterioration, and changes in the optic nerve discs, as well as by acromegaloid features. Of interest is the fact that the "café au lait" spots were noted shortly after the birth of the child. The onset of convulsions came about five years later. Bony changes were noted when the boy was about eight years of age, whereas the peripheral neuromas appeared only recently.

CASE 2.—D. W., a white girl, four years of age, was admitted to the Beth Israel Hospital on December 15, 1931, because of a marked swelling of four days' duration on the back of the left shoulder. The complete history, however, antedated considerably this present period of illness, for, during the previous year and up to about four weeks prior to admission to the hospital, the child had been subject to the irregular appearance of small tumors over the scalp and forehead. They were neither painful nor tender, lasted a short time, and disappeared of their own accord. They caused no impairment of the child's physical development or any change in her general behavior. At no time was there fever or other constitutional symptoms. An interval of about one month lapsed following the subsidence of the last swelling, when the mother noticed the presence of a new, rapidly growing mass over the posterior aspect of the girl's left shoulder. The swelling was much larger than any of those which had occurred previously, but again, there were no general symptoms, whereas locally there resulted only slight limitation of motion of the left arm and some stiffness of the neck.

As far as the child's developmental history is concerned, it was apparently normal in all respects. She was born at full term and weighed 5¼ pounds (2.38 kg.) at birth. The delivery was normal, respirations were spontaneous, and there were no convulsions. The child was breast fed for a period of five months and then was given cow's milk and the usual mixed diet. The trend of motor development proceeded normally. At four months, the child was able to support its head. She sat up erect at five months, crept at seven months, stood up supported at eight months, walked freely at fourteen months, and spoke single words at twelve months of age. The first tooth erupted at about six months. Aside from a bilateral suppurative cervical adenitis at two years of age, the child had always enjoyed good health.

The family history was essentially negative. The mother, thirty-one years of age, the father, forty years of age, and their only other child, a boy of twelve years, were all normal physically. There was no history of familial or hereditary diseases either in the maternal or paternal branches of the family.

Physical examination showed a quiet, mild-mannered, obedient little girl who was in no apparent pain or distress. The body temperature was 99.4° F., the pulse rate was 110, and respirations 28 per minute. She was well nourished and had good musculature and color. Her weight was 39½ (17.7 kg.) and her height 40 inches (101.6 cm.). The circumference of the head was 18¾ inches (47.6 cm.) and that of the chest 22¾ inches (57.8 cm.). Her neck and head were held in a protective posture and there was some limitation of motion of the former to the left. The left arm was favored and could neither be raised above the level of the shoulder nor rotated without resistance on the child's part. The pectoral and scapular groups of muscles on the left side seemed peculiarly spastic to palpation. Over the left shoulder was seen a large diffuse swelling which extended anteriorly outward and forward from the base of the neck to the supraclavicular area, and posteriorly, backward and downward to a point below the tip of the scapula. Laterally, it ex-



A *B*

Fig. 4.—*A*. Photograph taken on admission to hospital, showing the diffuse swelling of the left side of the back and of the left side of the neck. *B*. Showing the marked swelling of the left pectoral region occurring three months later.

tended from the spinal column to the posterior axillary line. (Fig. 4-*A* and *B*.) The mass was warm, firm, brawny, and slightly tender. Its edges were poorly defined and merged with the adjacent tissues. It was intimately attached to the underlying structures and to the overlying integument which was reddened, tense, and somewhat glossy. The superficial veins showed prominently. Comparative skin temperature determinations revealed little thermal difference between the swollen area and a symmetrical area on the opposite side. Directly below the large mass, a smaller, but similar, swelling was also present. There was some brawny edema of the suprapubic region. Elsewhere the skin was smooth, moist, and showed the usual growth of lanugo hair. There was no regional or general lymphadenopathy.

The head was symmetrical and the scalp, as well as the eyebrows and eyelashes, showed a good growth of soft, smooth, medium brown hair. The palpebral fissures

and the pupils were equal, the latter reacting promptly to light and accommodation. The eyegrounds were normal. The nose, mouth, throat, and ears showed nothing abnormal. All of the deciduous teeth had erupted; they were well formed, had good enamel, and showed no evidence of caries. As has been stated, the neck showed marked fullness on the left side. The trachea was in the midline; there were no abnormal pulsations. The heart, lungs, and abdomen were normal. The liver and spleen were not enlarged. The extremities were normal with the exception of limitation of motion of the left arm. The nails of the fingers and toes showed nothing unusual. Superficial and deep reflexes were equal and active; there were no abnormal reflexes.

The urine, blood counts, differential smears, and chemistry of the blood were normal. The Wassermann reaction of the blood and the von Pirquet test were negative. Roentgenograms of the chest, cervical and thoracic vertebrae, and of the left shoulder girdle revealed nothing of importance. Films of the skull showed changes suggesting an internal hydrocephalus. Bearing in mind the possibility that the swellings might have been allergic in origin, various protein sensitivity tests were done, but they gave no definite information.

During the early part of the child's stay in the hospital, the mass on the left side of the back, fluctuated in size, sometimes appearing smaller and being softer to touch, whereas at other times it was considerably larger and firmer. The limitation of motion of the left arm became more marked, as did the spasticity of the underlying groups of muscles. It was thought that microscopic examination of the tissue which formed the mass, would be of value in the diagnosis of the case. Accordingly a biopsy was done, the smaller swelling being excised under local anesthesia. The gross pathologic examination showed a piece of skin having a thick, glassy subcutaneous layer which measured about 1.4 centimeters in depth. Microscopically, the upper layers of the skin were normal; there was no trace of edema. The cutis was normal, as were the upper layers of subcutaneous fat. In the deeper tissues, however, there was seen a fibroma containing some nerve fibers at its periphery. (Fig. 5.) According to the report of the pathologist: "The tumor obviously belongs more to the fibromatous type of Recklinghausen's disease. Nerves are seen at its periphery. They are well separated from the surrounding tumor tissue. At low magnification, the interlacing of fibers immediately evokes the idea of neurofibroma. Throughout the tumor, thick, obviously fibrous, bands are seen stained intensely with the acid fuchsin. The remainder of the tumor consists of a fine reticulum which assumes an orange hue in the van Gieson stain. At many points it has a similarity with nervous tissue, but there is no definite proof. The many elongated, fairly light-staining nuclei show fibrillary prolongations at many points. Whether or not the reticulum has been formed by these cells cannot be stated. There are some groups of larger cells which are not characteristic of any definite histologic structure. No palisade arrangement of nuclei is seen. The tumor is situated way below the cutis; therefore nothing can be said about its relation to the sweat glands. Diagnosis: Neurofibromatous type of von Recklinghausen's disease."

After a period of observation, the child was discharged from the hospital. The swelling had subsided considerably, but the area remained indurated. The subsequent clinical course is of interest, in so far as new tumor masses appeared from time to time in different regions of the child's body. These swellings grew slowly, were similar in appearance and, after reaching their height of development, subsided gradually but never disappeared entirely. About one month following her discharge, the girl was seen in the follow-up clinic. Some swelling was still present on the left side of the back. There also seemed to be beginning involvement of the entire left pectoral area. The subcutaneous tissue was brawny to palpation. The left arm could not be raised voluntarily above the level of the shoulder; the underlying muscles were spastic. The right side of the back also showed evidence of in-

volvement, for just to the right of the spinal column, at the level of the lower thoracic vertebrae, a tumor measuring about 4 by 6 centimeters was visible. At the next examination, a month later, a new swelling was seen on the posterior aspect of the right side of the neck, causing considerable limitation of motion of the head. Shortly after a large mass developed over the left pectoral region. This swelling was again firm, warm, somewhat tender, and indefinitely demarcated from the surrounding tissues. At her last visit to the clinic, the child showed a recurrence of the swelling at the base of the left side of the neck. It was then learned that the child had entered another hospital for a period of observation. Information from that source showed that the disorder was also diagnosed as that of neurofibromatosis. Of interest is the fact that at this time roentgenograms of the various bones revealed many exostoses, some of which were associated with the tumor masses. Roentgen therapy was given, the tumors diminishing in size.

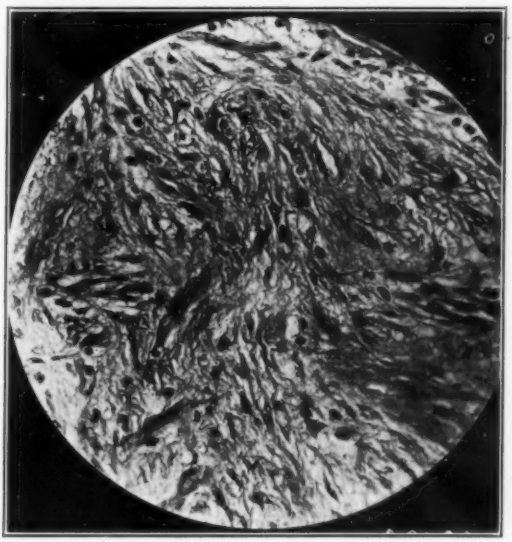


Fig. 5.—Photomicrograph of section of biopsy specimen. Note the thick interlacing fibrous bands and the fine reticular network.

Comment.—Case 2 is one of neurofibromatosis in a girl of four years, and is presented because of the unusual character and distribution of the cutaneous lesions, and because of the lack of constitutional symptoms. The history was that of the development of large indurated masses in the cervical, pectoral, scapular, lumbar, and pelvic regions of the body. These swellings were subject to marked fluctuations in size. Biopsy revealed the characteristic pathologic changes of neurofibromatosis. Subsequent roentgenographic examinations showed beginning osseous changes.

BOURNEVILLE'S TUBEROUS SCLEROSIS

Closely related to von Recklinghausen's neurofibromatosis, is the disorder which is known as tuberous sclerosis, a fairly rare congenital

malformation of ectodermal derivation, also affecting the brain, skin, and other organs of the body, and being associated invariably with epilepsy and feeblemindedness. It is sometimes known as "epiloia," a name proposed by Sherlock[17] in 1911. This term has been objected to by Babonneix[18] on the grounds that Sherlock merely redescribed and renamed the clinical picture of Bourneville's tuberous sclerosis.

Tuberous sclerosis was first described by Bourneville[19] in 1880. He reported the pathologic changes occurring in the brain of a three-year-old epileptic girl who presented clinically signs of arrested physical development, hemiplegia, idiocy, and "acne rosacea and pustulosis of the face." At necropsy, islets of hypertrophic sclerosis were found distributed over the cerebral hemispheres. The brain showed also an anomaly of the olivary bodies. Shortly after, Bourneville,[20] in collaboration with Brissaud, described another case in a four-year-old boy who suffered from convulsions. Autopsy revealed similar sclerotic lesions of the cerebral convolutions, in addition to a large hemorrhage in the right frontal lobe, arterial anomalies, and a congenitally malformed heart. However, it remained for Bundschuh[21] and for Bielschowsky and Gallus[22] to describe independently the minute histologic alterations occurring in the tumors of the brain in tuberous sclerosis.

Of interest are the cutaneous manifestations of tuberous sclerosis, the warty nodules occurring on the face and known as "adenoma sebaceum" or "nevus multiplex of Pringle." In 1890, Pringle[23] reported in a number of patients the presence of "indolent, firm, whitish, or yellowish, sago-grain-like, solid papules or little tumors, imbedded in the skin at different depths, or projecting from it . . . Intimately intermingled with these lesions and transgressing their limits in every direction, especially over the cheeks towards the ears, are innumerable capillary dilatations and stellate telangiectases." He recognized two elements in the face lesions, the one, a familiar, transitory form of "rosacea," and the other, an unfamiliar, permanent, neoplastic condition of the sebaceous glands, nevoid in character. He also noted that the eruption appeared to occur in subjects generally mentally below par. Pringle grouped these cases under the name of "adenoma sebaceum," but he gave due recognition to the fact that in 1885 Balzer[24] proposed the name in reporting a similar type of eruption of the face. He also made mention of an unpublished note by Hollopeau on a case of "sebaceous, miliary telangiectatic adenomata." Jadassohn[25] was the first, however, to appreciate the true significance of this anomalous condition of the skin and showed that it was neither an adenomatous nor a hyperplastic condition of the sebaceous glands. Rather, the lesions belong to the nevoid group of disorders and consist mainly of

hyperplastic connective and vascular tissues. They are part of the widely distributed disorder of tuberous sclerosis.

That tuberous sclerosis is a widespread systemic disorder, as was adduced by Kufs[26] in 1913, is evidenced by the fact that at autopsy gross abnormalities, such as cysts and tumors, are found in other internal organs. The kidneys and the heart are most frequently affected, although involvement of the pancreas, liver, and other organs may also occur. As has been reported by Koenen,[27] the disease may show hereditary and familial tendencies. It may be present at birth, or become manifest in early or even in late childhood. According to Yakovlev and Guthrie,[1] it is the most typical and clearly defined of the neurocutaneous syndromes in both its clinical and pathologic manifestations.

ENCEPHALOTRIGEMINAL ANGIOMATOSIS

It is a moot question whether the clinical picture of angiomatosis of the brain with vascular nevi of trigeminal distribution should be included in the so-called group of neurocutaneous syndromes. As Yakovlev and Guthrie[1] have stated: "Indeed the pathology of the vascular neurocutaneous syndrome, at first sight, obviously consists of congenital malformation of the blood vessels—a tissue, not of ectodermal, but of mesodermal, derivation." The authors present evidence, however, in favor of the neurogenic (ectodermal) origin of this vascular anomaly. They are of the opinion that ". . . . the blood vessels of the nervous system, of the skin, of the retina, and also certain of the glandular organs are the tissues of election for angiomatosis as compared, for example, to tissues of nonectodermal origin, such as bone and muscle." The distribution of the nevi corresponds, furthermore, apparently with zones of sympathetic innervation, suggesting that the vascular defect may have its origin in some maldevelopment of vasomotor origin. This fact receives added weight from the studies on the capillary circulation of the skin by Jaensch[28] who believes that the development of cutaneous capillaries is dependent in great degree upon the time of melanization of the nerves and the differentiation of the cerebral cortex. The work of Weber[29] has shown also that the telangiectatic, "port-wine" nevi are apparently neurogenic in nature. It should be emphasized that the mesodermal hyperplasia may be present in varying degrees in all three congenital disorders either as an accompanying condition or overshadowing entirely the ectodermal malformation.

In their monograph on tumors arising from blood vessels of the brain, Cushing and Bailey[30] state that these vascular newgrowths may be divided into two major groups, the angiomatous malformations and the angiomatous or true neoplasms of blood vessel elements. The angiotomatous malformations are due to some defect of develop-

ment and contain traces of compressed nerve between their vascular loops, thereby differentiating them from the blood vessel tumors proper, the angioblastomas, which are composed solely of mesodermal tissue. Angiomatous malformations may be predominantly capillary (telangiectatic), venous (angioma venosum), or arteriovenous (angioma arterialis) in their structure. Capillary malformations may occur in various parts of the brain, such as deep in the brain stem, and seldom give rise to symptoms, whereas the venous and arteriovenous angiomas are primarily surface lesions of the cerebral hemispheres, occasionally the hindbrain, and are often provocative of epileptiform seizures. At times, the angiomatous newgrowth extends with its apex toward the ventricle.

The venous angiomas are of interest in that they may be associated with nevi in the region of the distribution of the trigeminal nerve, a fact of importance in the early recognition of this form of vascular lesion, as compared with arterial angiomas whose presence are difficult of detection unless they are accompanied by an audible bruit or the secondary effects of aneurysmal communications giving rise to enlargement of extracranial vessels. At times, venous angiomas are associated with aneurysmal lesions and occasionally with unilateral exophthalmos. In recent years, Weber,[31] Dimitri,[32] Marque,[33] as well as others, have described cases in which congenital trigeminal nevi were found to be associated with calcified homolateral angiomas of the brain, usually in the occipital area. The majority of the cases occurred in young children in whom epilepsy, mental defect, and unilateral buphthalmus (or glaucoma) were outstanding features.

As has been previously stated, the angioblastomas are true vascular neoplasms and are to be clearly differentiated from the angiomatous malformations. According to Cushing and Bailey,[30] angioblastomas are rarely, if ever, accompanied by nevi. They are usually found in the cerebellum, occasionally in the medulla oblongata or in the cord, and they may be either cystic or solid in structure. They were first described in 1926 by Lindau[34] who recognized their true nature while making a study of cysts of the cerebellum. Microscopically, the angioblastomas show a sharp demarcation between the tumor proper and the surrounding nerve tissue and exhibit a marked tendency toward cyst formation. Lindau found also that the angioblastomas are frequently accompanied by concomitant malformations or tumors of somatic organs, such as cysts of the kidneys and pancreas. In addition there may occur vascular newgrowths of the retina.

The angiomas of the retina alone have long been known by ophthalmologists under the name of von Hippel's disease.[35] However, they were really first recognized in 1894 by Treacher Collins[36] who described two cases, in brother and sister, presenting peculiar vascular newgrowths affecting the retinal structure of both eyes. Collins

wrote that: "It was made up of a plexus of numerous very thin-walled blood vessels and there are in it cystic spaces. It may, therefore, best be described as a capillary nevus, which in places has undergone cystic degeneration." According to Lindau,[37] 25 per cent of the cases of von Hippel's disease give rise to symptoms of brain complications and 20 per cent of the cases have been found to be familial. Møller[38] has called attention to the familial nature of the disease, and Rochat[39] has published his experiences with one family in which the factor of heredity was demonstrable for three generations.

In a recent symposium on the problem of vascular newgrowths of the brain, Lindau[37] stated that:

> I have adduced good evidence that the subdivisions of the vascular newgrowths into two major groups, angiomatous malformations and hemangioblastomas, have been well established and means a great improvement, both clinically and pathologically. Further I have shown that each of these groups includes a general systemic disorder, the first a cavernous angiomatosis of the brain and skin, associated with buphthalmus, but no underlying angioma causing eye lesion, and the second, a capillary angiomatosis of the cerebellum and the retina with coordinated lesions of the abdominal organs. Thus both these systemic disorders, although related and rather alike, clearly differ, and as we have never met with a coincidental occurrence of these two conditions in the same family, it would be better at the present stage not to mix them up.

Case 3 is presented as an example of the clinical picture of calcified cavernous or venous angioma of the brain associated with nevi in the region of distribution of the trigeminal nerve. The pathologic features of this case have been considered elsewhere by Brock and Dyke.[40]

Case 3.—S. L., a white boy, was born at full term on May 12, 1925. The delivery was normal; there were no convulsions. The mother, a multipara, was thirty-four years of age, physically normal, and throughout pregnancy had suffered no illnesses. Her first two pregnancies terminated in miscarriages at three months. Subsequently she was delivered of four normal children. The father was thirty-nine years of age, and, at about this time, was treated surgically for a gastric ulcer. The family history was essentially negative.

At birth, the infant weighed 7 pounds (3.18 kg.). He was nursed for about sixteen months, and in addition, from six months on, received cereals, fresh vegetables, and orange juice daily, but no cod liver oil. At about four months, the infant was able to hold up its head. He sat up erect at six months, and stood up supported at about eight months, but did not pass through either the crawling or creeping stages of motor development. Walking was delayed markedly until about four years of age. The reason for this retardation will be explained subsequently. The first tooth erupted at five months. Babbling began at six months of age, but the development of speech never progressed beyond this rudimentary stage. Early perceptual and social development followed apparently a normal trend. At approximately six months of age, the child showed signs of recognizing and smiling at the various members of the family. He was also able to distinguish between strangers and friends.

The first period of illness occurred when the infant was nine months of age. He was then admitted to the Beth Israel Hospital with a history of three days' duration, characterized by convulsions and weakness of the right upper and lower

extremities. On admission, the temperature was 105° F. There was drowsiness, nystagmus of both eyes, and clonic contractions of the right side of the body. A nevus was also noticed on the right side of the forehead, but its full significance was not realized at this time. The left ear showed a purulent otitis media. The fundi of both eyes appeared to be normal, but it was noted by the ophthalmologist that the infant did not react promptly to the influence of light. A spinal puncture was attempted, but a bloody fluid was obtained. The Wassermann reaction of the blood was negative. With the subsidence of the acute symptoms, the infant showed a complete paralysis of the right upper and lower extremities. After a period of convalescence, he was discharged from the hospital, his condition having been diagnosed as that of polioencephalitis.

For the next two years the child was observed in the follow-up clinic. During this time, he was subject to attacks of convulsions which occurred at irregular intervals and which were accompanied by brief periods of unconsciousness. Occasionally the child had several convulsive seizures a day, whereas at other times

Fig. 6.—"Port-wine" nevus of the right side of the forehead and face in the regions of distribution of the first and second branches of the trigeminal nerve.

many weeks intervened between attacks. He was irritable, restless, and slept poorly. He lacked urinary control and soiled himself frequently. General motor and manipulatory control was greatly retarded. The weakness of the right upper and lower extremities showed only slight improvement. Apparently, he understood gestures and spoken commands, and he was amenable to discipline. It was also observed that although he reacted to stimulation from bright lights, his sense of perception was poor. It is interesting to note in this connection that improvement was noted in tactile sensitivity and in the appreciation of the attributes of space. Hearing appeared to be normal.

At six and one-half years of age, the boy was readmitted to the hospital in order to ascertain whether the nevus of the face was associated with a similar vascular lesion of the central nervous system. He now weighed 56 pounds (25.4 kg.) and was 43½ inches (110.5 cm.) in height. The circumference of his head was 19½ inches (49.5 cm.) and that of his chest 28 inches (71.1 cm.). He was well nourished, had good subcutaneous fat and the mucous membranes were of good color. With the exception of the paralyzed limbs, the musculature was firm. His general attitude and behavior was that of the idiot. In bed, he tossed from side to side, hitting

his head or face with his hands or holding his fingers in his mouth. He uttered peculiar, meaningless sounds. It was impossible to attract or to hold his attention. When erect, his weight was thrown upon the right lower extremity; his right foot was held everted. The right hip was flattened and there was a compensatory scoliosis of the lumbar spine to the left side. When assisted, he walked by stepping forward on the left foot, then dragging the right foot up to meet it.

The skin was moist and coarse and showed a normal growth of lanugo hair. The hair of the scalp, eyebrows, and eyelashes was straight, coarse, and medium brown. It may be noted here that the nails of the fingers and of the toes were normal. The head appeared to be smaller than normal and was definitely flattened on the left side posteriorly. The right side of the face was larger than the left side. On the right side of the forehead, there was seen a large, raised, "port-wine" nevus, vivid red in hue and irregularly oblong in shape, measuring approximately 11 centimeters in length and 4 centimeters in width. (Fig. 6.) It began just beneath the hair line and ran obliquely downward and inward to the bridge of the nose, then spread out irregularly over the right upper eyelid. A similar but smaller nevus of irregular shape was also present on the right side of the upper lip, and an additional one of oval shape and about 5 centimeters in its longest diameter, on the left vertex area of the scalp.

The right palpebral fissure was narrower than the left. The pupils were regular and reacted normally to light. The eyegrounds could not be examined properly. The ears were normal. The nose was flattened at the bridge; its base was broad. There was no obstruction to nasal breathing. The lips were thickened, but the vermilion borders were well defined. The incisor teeth of the upper jaw protruded prominently; the lower jaw receded markedly. Ten permanent teeth had erupted and of these, all four first molars showed advanced caries. The enamel was fair. All remaining deciduous teeth showed marked disintegration, the stumps being stained brownish black. The tongue was normal and protruded in the midline. The neck was normal. There was no lymphadenopathy.

The chest was symmetrical; both nipples were normal. The heart and lungs were normal. Neither the liver nor spleen was palpable. No abdominal masses were present. The genitals were normal in size and the testicles fully descended. Both the right upper and lower extremities showed spastic paralysis and considerable muscular atrophy. However the fingers of both hands were flaccid and could be extended backwards easily. There was definite shortening of the paralyzed limbs. All deep reflexes were hyperactive on the right side. The right abdominal and cremasteric reflexes were diminished and there was a right-sided Babinski reversal, as well as a prolonged ankle clonus. The skin was hyperesthetic.

In view of the history of convulsions, progressive mental deterioration, and physical signs of central nervous system involvement, together with the presence of the extensive nevus on the forehead, a clinical diagnosis was made of angiomatous tumor of the brain associated with a nevus of the forehead in the region of the distribution of the trigeminal nerve. Encephalography substantiated the diagnosis (Figs. 7-*A*, *B*.). The cranial cavity was relatively small, but the bones were of normal thickness. The diploetic layer was normal. There were no evidences of increase in intracranial pressure except that the floor of the middle fossa was somewhat depressed and narrow. The sella turcica was small. There was no diastasis of the sutures or of the fontanelles. The cerebral pathways were normal in size, but were slightly diminished in number; they extended well forward over the frontal area on the right side, but were obliterated on the left side. There was defective outlining of the ventricles and, on the left side, a porencephalic cyst communicated with the ventricle. The cranial contents were shifted to the left side. The basal cisterna could not be visualized except for an area in the region of the cisterna

A

B

Fig. 7.—*A*. Encephalograms showing the linear calcific deposits in the blood vessels of the right occipital lobe, as well as the porencephalic cyst on the left side. Note the shifting of the cranial contents to the left side.

pontis. There were irregular linear calcifications extending from the region of the lambdoid suture to that of the sella turcica. These calcifications were apparently in the blood vessels of the occipital lobe of the brain.

Comment.—Case 3 occurring in a boy six and one-half years of age, is illustrative of the encephalotrigeminal variety of vascular neurocutaneous syndrome. Outstanding in the history is the cerebral injury suffered by the boy at nine months of age, leading to right-sided hemiplegia, subsequent mental defectiveness, and the frequent occurrence of epileptiform seizures. Clinically, the boy showed an extensive "port-wine" nevus of the right side of the forehead and face. Encephalography revealed calcific deposits in the right occipital lobe of the brain, as well as a porencephalic cyst of the left side.

SUMMARY

Attention is directed to a group of three unusual congenital disorders to which surprisingly little reference has been made in the pediatric literature. The disorders are von Recklinghausen's neurofibromatosis, Bourneville's tuberous sclerosis, and angiomatosis of the brain associated with vascular nevi in the region of the distribution of the trigeminal nerve. All three conditions have been classified in the general category of neurocutaneous syndromes, after the suggestion of French observers. Recently, Yakovlev and Guthrie[1] have proposed that the diseases be designated by the more descriptive term of "congenital ectodermoses."

All three congenital disorders exhibit marked similarity in their clinical manifestations and in the character and distribution of their pathologic features. Furthermore, they involve electively organs, such as the nervous system, skin, retina, and eyeball, having their common origin in the ectodermal layer of the developing blastoderm. It should be borne in mind, however, that mesodermal hyperplasia, as is evidenced by the frequent presence of vascular nevi, may occur in varying degrees in all three congenital disorders either as a concomitant condition or obscuring entirely the ectodermal malformation.

Although all three syndromes show individual and characteristic manifestations, they are by no means mutually exclusive. They present signs and symptoms which overlap greatly and which exhibit an impressive range of variability. Of clinical interest is the occurrence of characteristic cutaneous anomalies which are indicative of associated maldevelopments in deeper seated, embryologically related structures, such as the peripheral and central nervous systems, and which affect usually the cephalic and caudal ends of the body. The cutaneous manifestations are not purely localized lesions, but are the external expressions of widespread systemic maldevelopments which affect visceral, as well as somatic, structures. This is evidenced by the fact that at autopsy gross abnormalities, such as cysts and tumors, are found

in other internal organs. Also of importance in this group of congenital disorders is the involvement of the entire nervous system and, in addition, the frequent occurrence of epilepsy and feeblemindedness. All three neurocutaneous syndromes show, furthermore, definite familial or hereditary tendencies.

Von Recklinghausen's neurofibromatosis is a generalized disease involving primarily nervous tissue in any part of the body with secondary changes in other organs. Characteristically there may occur polypoid tumors of the skin, subcutaneous nodular tumors of the peripheral nerve trunks, lesions of the central nervous system and of the meninges, brownish pigmentation of the skin ("café au lait" spots), secondary changes in the skeletal system, and abnormalities of development of visceral structures. The disorder is not seen always in its complete form, various incomplete or abortive forms being present in which only one of the cardinal signs is manifest.

Bourneville's tuberous sclerosis is a fairly rare congenital malformation and it is probably the most typical and clearly defined of the neurocutaneous syndromes in its clinical and pathologic features. It is a widespread disorder showing islands of hypertrophic sclerosis of the cerebral hemispheres, warty nodules of the face, the so-called "adenoma sebaceum," and cysts and tumors of internal organs. It is invariably associated with epilepsy and mental defect.

The last of the group of neurocutaneous syndromes, is the clinical picture of angiomatosis of the brain associated with vascular nevi in the region of distribution of the trigeminal nerve (encephalotrigeminal angiomatosis). Although, at first sight, it consists of congenital malformation of blood vessels, a tissue of mesodermal origin, evidence is in favor of the fact that it is of neurogenic (ectodermal) origin. It should be emphasized that vascular newgrowths of the brain are divisible into two major groups, the angiomatous malformations which consist of nervous and vascular tissue, and the angioblastomas or true neoplasms which are composed solely of mesodermal tissue. The latter involve primarily the cerebellum and have been known under the name of Lindau's disease. They may be either solid or cystic in structure and are accompanied frequently by malformations of visceral organs and vascular newgrowths of the retina (von Hipple's disease), but no nevi of the skin. This condition should be clearly differentiated from the angiomatous malformations which are also accompanied by general systemic malformations and by vascular nevi of the skin, as well as buphthalmus (glaucoma). Often the congenital nevi of trigeminal distribution are associated with calcified homolateral angiomatous malformations of the brain, usually of the occipital area.

Three case reports have been presented, two of them as illustrations of the varied clinical manifestations of the complicated disorder of von

Recklinghausen's neurofibromatosis, and one of them as an example of angiomatous malformation of the brain in association with vascular nevi of trigeminal distribution.

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DETERMINING APPROPRIATE WEIGHT FOR BODY BUILD*

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NUTRITIONAL status has long held first place as a measure of health, and rightly so; but modern ideas of judging nutrition are changing rapidly. We know that there is a proper weight range for each child which reflects his optimum development and state of health. This proper weight depends on body build or relative width of the body as well as on height and age.

Previous studies by Gray,[1] Franzen,[2] Miles,[3] and others have shown the relationship between various body widths and weight. Gray in 1928 proved statistically that the physical traits most highly correlated with weight were first stature, then bicristal diameter, third age, then bistyloid, then biacromial diameter, and sixth bimalleolar diameter. Gray's material consisted of 810 private school boys aged four to twenty years. He concludes: "that weight is best referred to stature, next best to bicristal diameter, only third best to age, while wrist diameter is not worth further consideration. . . . Hence it may be expected that the multiple correlation of weight with stature and bicristal diameter will be better than with stature and age."

The importance of a mathematical appraisal of observed variability was suggested by Faber[4] in 1925. We attempted this in measuring the relationship of width to weight when both were expressed in terms of percentage deviation from the mean for the age sex group.

Dublin and Gebhart[5] showed that present standards failed to identify a large proportion of undernourished Italian children. Turner[6] has shown that many underweight children are not malnourished and that a perfectly healthy child may be thin because he has inherited a slender skeleton. He concludes that the skeletal type of the child should be judged as a basis for interpreting the underweight data. Clark, Sydenstricker and Collins[7] found that a fairly large percentage of well-nourished native white children were more than 10 per cent underweight according to the Baldwin-Wood tables and they suggest that deviation from average weight need not be a criterion of physical fitness and may not be a matter of ill health or malnutrition. Consideration of body build seems to reconcile these statements with the assumptions upon which the Baldwin-Wood tables are based.

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In Faber's thorough statistical study of the heights and weights of 60,000 San Francisco school children, he found that for subgroups consisting of from 400 to 600 members the mode corresponded very closely with the Baldwin-Wood standards. For this reason we have based our height-weight table for different body builds on the Baldwin-Wood table, which established average weight for average build. Then deviation from average build determines deviation from average weight.

Faber showed an increase in weight variability with age in both sexes and a marked difference between boys and girls. Our measurements show a corresponding increase in variability of diameters with age for both sexes and a marked difference in boys and girls beginning at adolescence.

The width-length index of body build as described by Lucas and Pryor[8] makes use of stature and bicristal diameter to designate types of build and also as a basis for weight prediction. The bicristal (or bi-iliac) diameter divided by the standing height multiplied by 100 gives the width-length index and is a measure of the relative width of the body. They have followed the technic of Miles and Gray, in using firm pressure to get as nearly as possible measurements of the widest flare of the iliac crests. For this purpose sliding anthropometric calipers are the most satisfactory, although spreading calipers may be used.* Other body measurements were done as described by Hrdlicka[9] and adopted by the International anthropometric agreement.

Our width-length indices parallel Gray's bicristal-stature indices at all ages and for both sexes and are consistently a little smaller. The bicristal diameter appears to be 0.6 cm. (0.25 in.) less in our series than in Gray's series which may be explained on a basis of superior social economic status in Gray's private school children, since the bicristal diameters obtained by us on our own small series of 300 private school boys are practically identical with Gray's.

The bi-iliac diameter can be measured more accurately than chest width or shoulder width because it is not affected by respiratory movements or changes in posture. The greater accuracy of the pelvic measurement is shown when two or more observers measure the same children consecutively. It was found at the Institute of Child Welfare, for example, that for two physicians the average difference in measurement of 112 adolescent children was as follows:

Bi-iliac	56 girls	2.3 mm. or % error	0.99 ± 0.05
"	56 boys	2.6 " " " "	1.16 ± 0.05
Biacromial	56 girls	4.7 " " " "	1.49 ± 0.05
"	56 boys	4.1 " " " "	1.36 ± 0.05
Lateral Chest	56 girls	3.8 " " " "	1.70 ± 0.05
" "	56 boys	4.9 " " " "	2.10 ± 0.10

*The wooden sliding caliper made by the Marine Compass Company of Hanover, Mass., proved a satisfactory instrument and is far less expensive than the standard anthropometric metal caliper.

Todd[10] reported that measurements on the living body need not vary more than 5 to 10 millimeters. Dahlberg[11] reports an average difference in millimeters for various measurements as follows: bicristal 1.64; biacromial 3.31, and stature 3.56. Gray reports the difference expected and the difference accepted in his work for various measurements in millimeters as follows: bicristal 1-2; stature and biacromial 2-4; and chest measurements 2-10.

It seems, then, that the bicristal diameter is the width measurement of choice because it is more constant than any chest measurement, is not affected by respiration, and may be more accurately determined.

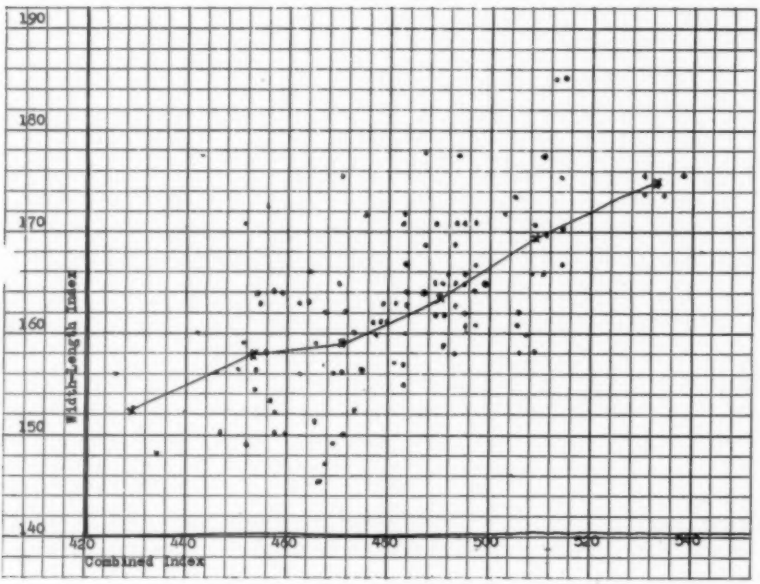

Fig. 1.—Width-length index plotted against combined index. One hundred and three girls, ages ten, eleven, and twelve years.

Various complicated indices of body build have been advocated, each involving several body measurements of girths and diameters. In order to see what additional information could be had from a more complicated index of build, we have plotted a combined index against the width-length index for 100 boys and 100 girls aged ten to twelve years. (See Figs. 1 and 2.) The combined index consisted of biacromial diameter plus lateral chest diameter, plus anteroposterior chest diameter divided by stature multiplied by 100. A comparison of these chest and shoulder measurements with the single width of hips, each in percentage of standing height, shows that the single width-length index makes practically the same classification of body build as the more complicated one for the group, and is more accurately and more

easily determined. In certain individual instances where there is a lack of symmetry between pelvic and thoracic development there would be differences in the results obtained by these two methods of classification, but we think this occurs infrequently.

The relationship between relative width of the body (as measured by the width-length index) and body weight was worked out first on 1000 children from Dr. Lucas' private practice. It was found that the standard deviation from average weight, referred to the Baldwin-Wood table, was approximately double the standard deviation from

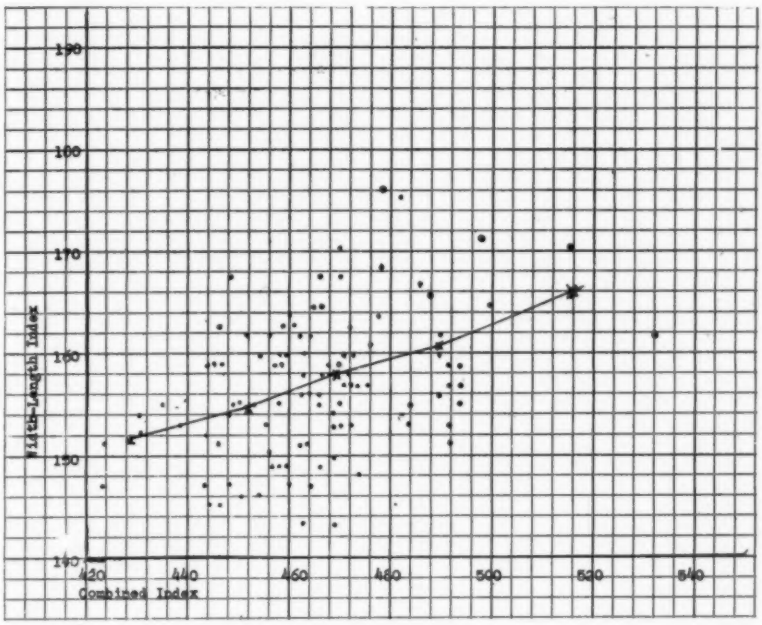

Fig. 2.—Width-length index plotted against combined index. One hundred and three boys, ages ten, eleven, and twelve years.

the mean width-length index for each age sex group, when both were expressed in percentage. The study was then extended to include 2000 public school children in San Francisco, Oakland, and San Mateo; 700 clinic patients at the University of California Hospital; 300 clinic patients at Childrens Hospital, San Francisco; 300 private school boys at the Menlo School and Junior College; 200 children in the adolescent study at the Institute of Child Welfare, Berkeley; and 60 children studied in a private research by Dr. R. O. Moody at the University of California. Children in the endocrine clinics were excluded as were all others with serious or chronic illnesses.

Our total series of 4560 cases was divided into age sex groups for study. The same relationship between standard deviations from width and weight was found to hold for both the large series and the small series. Those width-length indices which are smaller than the mean distinguish slender-built children and the indices above the mean distinguish broad-built or stocky children. A slender-built child

TABLE I

WIDTH-WEIGHT TABLE FOR GIRLS*

SIX TO SIXTEEN YEARS

Height in Inches	Six years							Seven years						
	15.5 cm. 6.1 in.	16.5 6.5	17.0 6.7	18.3 7.2	19.6 7.7	20.1 7.9	21.1 cm. 8.3 in.	16.2 cm. 6.4 in.	17.2 6.8	17.7 7.0	19.0 7.5	20.3 8.0	20.9 8.2	21.8 cm. 8.6 in.
38	26	27	28	31	34	35	36	28	30	31	34	37	38	40
39	26	28	29	32	35	36	38	29	31	32	35	38	39	41
40	28	30	31	34	37	38	40	31	33	34	37	40	41	43
41	29	31	32	35	38	39	41	32	34	36	39	41	44	46
42	31	33	34	37	40	41	43	33	35	37	40	43	45	47
43	32	34	35	39	41	44	46	36	38	39	43	47	48	50
44	33	35	37	40	43	45	47	37	40	41	45	49	50	53
45	36	38	39	43	47	48	50	40	43	44	48	52	53	56
46	37	40	41	45	49	50	53	42	44	46	50	54	56	58
47	40	43	44	48	52	53	56	44	46	48	52	56	58	61
48	42	44	46	50	54	56	58	45	48	50	54	58	60	63
49	43	46	48	52	56	58	61	48	51	52	57	62	63	66
50	45	48	50	54	58	60	63	51	54	56	61	66	68	71
51								54	57	59	64	69	71	74
52														
53														

Height in Inches	Eight years							Nine years						
	17.2 cm. 6.8 in.	18.3 7.2	18.8 7.4	20.3 8.0	21.8 8.6	22.3 8.8	23.4 cm. 9.2 in.	18.1 cm. 7.1 in.	19.1 7.5	19.6 7.7	21.1 8.3	22.6 8.9	23.1 9.1	24.1 cm. 9.5 in.
42	31	33	34	37	40	41	43	37	39	40	44	48	49	51
43	32	34	36	39	41	44	46	38	41	42	46	50	51	53
44	35	37	38	42	46	47	49	40	43	44	48	52	53	56
45	37	39	40	44	48	49	51	43	45	47	51	55	57	59
46	38	41	42	46	50	51	53	44	47	49	53	57	59	62
47	40	43	44	48	52	53	56	47	50	51	56	61	62	65
48	43	45	47	51	55	57	59	49	52	54	59	64	66	69
49	44	47	49	53	57	59	62	52	55	57	62	67	69	72
50	47	50	51	56	61	62	65	54	58	60	65	70	72	76
51	49	52	54	59	64	66	69	57	61	63	68	73	75	79
52	52	55	57	62	67	69	72	59	62	65	70	75	78	81
53	54	58	60	65	70	72	76	62	66	68	74	80	82	86
54	57	61	63	68	73	75	79	65	69	71	77	83	85	89
55	59	62	65	70	75	78	81	68	72	75	81	87	90	94
56	61	65	67	73	79	81	85							
57														
58														

Height in Inches	Ten years							Eleven years						
	18.8 cm. 7.4 in.	19.8 7.8	20.6 8.1	22.1 8.7	23.6 9.3	24.4 9.6	25.4 cm. 10.0 in.	19.6 cm. 7.7 in.	20.9 8.2	21.6 8.5	23.1 9.1	24.6 9.7	25.4 10.0	26.7 cm. 10.5 in.
47	40	43	44	48	52	53	56	43	45	47	51	55	57	59
48	43	45	47	51	55	57	59	45	48	50	54	58	60	63
49	45	48	50	54	58	60	63	49	52	54	59	64	66	69
50	48	51	52	57	62	63	67	51	54	56	61	66	68	71
51	49	52	54	59	64	66	69	53	56	58	63	68	70	73
52	52	55	57	62	67	69	72	55	59	61	66	71	73	77
53	55	59	61	66	71	73	77	58	61	64	69	74	77	80
54	57	61	63	68	73	75	79	60	64	66	72	78	80	84
55	60	64	66	72	78	80	84	64	68	70	76	82	84	88
56	64	68	70	76	82	84	88	67	71	74	80	86	89	93
57	67	71	74	80	86	89	93	71	75	78	84	90	93	97
58	69	73	76	82	88	91	95	74	79	81	88	95	97	102
59	72	76	78	85	92	94	98	78	83	86	93	100	103	108
60	75	79	82	89	96	99	103	82	87	90	97	104	107	112
61								86	91	94	102	110	113	118
62														

*Weight in pounds (without clothing).

has small bones and should weigh less than a broad-built child of the same age and height. The width-length index measures the bony framework or body build and provides the basis for calculating the deviation from average weight.

TABLE I—CONT'D*

Height in Inches	Twelve years							Thirteen years						
	20.6 8.1	21.6 8.5	22.3 8.8	24.1 9.5	25.9 10.2	26.6 10.5	27.6 cm. 10.9 in.	21.3 8.4	22.6 8.9	23.3 9.2	25.1 9.9	26.9 10.6	27.6 10.9	28.9 cm. 11.4 in.
50	50	53	55	60	65	67	70	58	61	64	69	74	77	80
51	53	56	58	63	68	70	73	60	63	65	71	77	79	82
52	54	58	60	65	70	72	76	63	67	69	75	81	83	87
53	56	60	62	67	72	74	78	66	70	73	79	85	88	92
54	58	61	64	69	74	77	80	69	73	76	82	88	91	95
55	61	65	67	73	79	81	85	72	77	79	86	93	95	100
56	65	69	71	77	83	85	89	76	80	83	90	97	100	104
57	67	71	74	80	86	89	93	80	85	88	95	102	105	110
58	71	75	78	84	90	93	97	83	88	92	99	106	110	115
59	74	79	81	88	95	97	102	88	93	96	104	112	115	120
60	78	83	86	93	100	103	108	91	97	100	108	116	119	125
61	83	88	91	98	105	108	113	95	101	105	113	121	125	131
62	87	92	95	103	111	114	119	100	106	109	118	127	130	136
63	91	97	100	108	116	119	125	103	109	113	122	131	135	141
64	95	100	104	112	120	124	129	106	113	117	126	135	139	146
65	98	104	107	116	125	128	134	109	115	119	129	139	143	149
66														
67														
68														

Height in Inches	Fourteen years							Fifteen years						
	21.8 8.6	23.1 9.1	23.9 9.4	25.6 10.1	27.3 10.8	28.1 11.1	29.4 cm. 11.6 in.	22.3 8.8	23.6 9.3	24.4 9.6	26.2 10.3	28.0 11.0	28.8 11.3	30.0 cm. 11.8 in.
55	64	68	70	76	82	84	88	76	80	83	90	97	100	104
56	68	72	75	81	87	90	94	79	84	87	94	101	104	109
57	72	77	79	86	93	95	100	83	88	91	98	105	108	113
58	77	81	84	91	98	101	105	87	92	95	103	111	114	119
59	79	84	87	94	101	104	109	89	95	98	106	114	117	123
60	83	88	92	99	106	110	115	94	99	103	111	119	123	128
61	87	92	95	103	111	114	119	96	102	105	114	123	126	132
62	90	96	99	107	115	118	124	99	105	108	117	126	129	135
63	95	98	102	110	118	122	127	101	107	111	120	129	133	139
64	97	103	106	115	124	127	133	104	110	114	123	132	136	142
65	100	106	110	119	128	132	138	109	115	119	129	139	143	149
66	103	109	113	122	131	135	141	112	119	123	133	143	147	154
67	108	115	118	128	138	141	148	114	121	125	135	145	149	156
68	111	117	121	131	141	145	151	115	122	126	136	146	150	157
69	112	119	123	133	143	147	154	117	124	128	138	148	152	159
70	113	120	124	134	144	148	155							
71	115	122	126	136	146	150	157							

Height in Inches	Sixteen years							
	22.9 9.0	24.1 9.5	24.9 9.8	26.6 10.5	28.4 11.2	29.2 11.5	30.5 cm. 12.0 in.	
59	74	79	81	88	95	97	102	
60	79	84	87	94	101	104	109	
61	85	90	93	101	109	112	117	
62	89	94	97	105	113	116	121	
63	94	99	103	111	119	123	128	
64	97	103	106	115	124	127	133	
65	101	107	111	120	129	133	139	
66	106	113	117	126	135	139	146	
67	111	118	122	132	142	146	153	
68	114	121	125	135	145	149	156	
69	119	126	131	141	151	156	163	
70	121	128	132	143	154	158	165	
71	126	133	138	149	160	165	172	
72	129	137	142	153	164	169	177	
73	134	142	146	158	170	174	182	
74	137	145	150	162	174	179	187	

Directions: Take age at nearest birthday, and height at nearest inch. Measure the bi-iliac diameter and match it with the nearest diameter for the proper age shown along the top of the table. Appropriate weight for build is read for the given height at that width.

*Weight in pounds (without clothing).

For the convenience of physicians we have constructed Tables I and II showing appropriate weights for body build based on the two physical traits, height and bicristal diameter, which Dr. Gray found correlated most highly with weight, and taking into consideration age which correlated third. We have called these Width-Weight tables. The Baldwin-Wood table was used to determine average height and

TABLE II

WIDTH-WEIGHT TABLE FOR BOYS*

SIX TO SIXTEEN YEARS

Height in Inches	Six years							Seven years						
	15.7 cm. 6.2 in.	16.7 6.6	17.2 6.8	18.5 7.3	19.8 7.8	20.3 8.0	21.3 8.4	16.2 cm. 6.4 in.	17.3 6.8	18.0 7.1	19.3 7.6	20.6 8.1	21.3 8.4	22.4 8.8
38	26	28	29	32	35	36	38	30	32	33	36	39	40	42
39	27	29	30	33	36	37	39	31	33	34	37	40	41	43
40	28	30	31	34	37	38	40	32	34	36	39	41	44	46
41	30	32	33	36	39	40	42	35	37	38	42	46	47	49
42	31	33	34	37	40	41	43	37	39	40	44	48	49	51
43	32	34	36	39	41	44	46	38	41	42	46	50	51	53
44	35	37	38	42	46	47	49	40	43	44	48	52	53	56
45	37	39	40	44	48	49	51	43	45	47	51	55	57	59
46	38	41	42	46	50	51	53	44	47	49	53	57	59	62
47	40	43	44	48	52	53	56	47	50	51	56	61	62	65
48	42	44	46	50	54	56	58	49	52	54	59	64	66	69
49	44	47	49	53	57	59	62	51	54	56	61	66	68	71
50	46	49	51	55	59	61	63	54	57	59	64	69	71	74
51														
52														
53														
54														
55														
56														

Height in Inches	Eight years							Nine years						
	17.2 cm. 6.8 in.	18.3 7.2	18.8 7.4	20.3 8.0	21.8 8.6	22.3 8.8	23.4 9.2	18.1 cm. 7.1 in.	19.1 7.5	19.6 7.7	21.1 8.3	22.6 8.9	23.1 9.1	24.1 9.5
42	31	33	34	37	40	41	43	37	39	40	44	48	49	51
43	32	34	36	39	41	44	46	38	41	42	46	50	51	53
44	35	37	38	42	46	47	49	40	43	44	48	52	53	56
45	37	39	40	44	48	49	51	43	45	47	51	55	57	59
46	38	41	42	46	50	51	53	44	47	49	53	57	59	62
47	40	43	44	48	52	53	56	47	50	51	56	61	62	65
48	43	45	47	51	55	57	59	49	52	54	59	64	66	69
49	44	47	49	53	57	59	62	52	55	57	62	67	69	72
50	47	50	51	56	61	62	65	54	58	60	65	70	72	76
51	49	52	54	59	64	66	69	57	61	63	68	73	75	79
52	52	55	57	62	67	69	72	59	62	65	70	75	78	81
53	54	58	60	65	70	72	76	62	66	68	74	80	82	86
54	57	61	63	68	73	75	79	65	69	71	77	83	85	89
55	59	62	65	70	75	78	81	68	72	75	81	87	90	94
56	61	65	67	73	79	81	85							
57														
58														

Height in Inches	Ten years							Eleven years						
	18.3 cm. 7.2 in.	19.3 7.6	20.1 7.9	21.6 8.5	23.1 9.1	23.9 9.4	24.9 9.8	19.0 cm. 7.5 in.	20.0 7.9	20.8 8.2	22.3 8.8	23.8 9.4	24.6 9.7	25.6 10.1
47	40	43	44	48	52	53	56	44	47	49	53	57	59	62
48	43	45	47	51	55	57	59	47	50	51	56	61	62	65
49	44	47	49	53	57	59	62	49	52	54	59	64	66	69
50	47	50	51	56	61	62	65	52	55	57	62	67	69	72
51	49	52	54	59	64	66	69	54	58	60	65	70	72	76
52	52	55	57	62	67	69	72	57	61	63	68	73	75	79
53	54	58	60	65	70	72	76	60	63	65	71	77	79	82
54	57	61	63	68	73	75	79	63	67	69	75	81	83	87
55	60	63	65	71	77	79	82	66	70	73	79	85	88	92
56	63	67	69	75	81	83	87	69	73	76	82	88	91	95
57	66	70	72	78	84	86	90	72	77	79	86	93	95	100
58	69	73	76	82	88	91	95	76	80	83	90	97	100	104
59	72	76	78	85	92	94	98	78	83	86	93	100	103	108
60	75	79	82	89	96	99	103	83	88	91	98	105	108	113
61								87	92	95	103	111	114	119
62														
63														

*Weight in pounds (without clothing).

weight for each age sex group. The Underweight Reference tables compiled by the American Child Health Association in 1924 were used to determine 7-10-15 per cent under average weight for each age and height. The percentages over average weight were calculated directly from these.

TABLE II—CONT'D*

Height in Inches	Twelve years							Thirteen years						
	19.8 cm. 7.8 in.	20.8 8.2	21.6 8.5	23.1 9.1	24.6 9.7	25.4 10.0	26.4 cm. 10.4 in.	20.3 cm. 8.0 in.	21.3 8.4	22.1 8.7	23.6 9.3	25.1 9.9	25.9 10.2	26.9 cm. 10.6 in.
50	47	50	51	56	61	62	65	52	55	57	62	67	69	72
51	49	52	54	59	64	66	69	55	59	61	66	71	73	77
52	52	55	57	62	67	69	72	58	61	64	69	74	77	80
53	55	59	61	66	71	73	77	60	64	66	72	78	80	84
54	58	61	64	69	74	77	80	64	68	70	76	82	84	88
55	60	64	66	72	78	80	84	67	71	74	80	86	89	93
56	63	67	69	75	81	83	87	70	74	77	83	89	92	96
57	66	70	73	79	85	88	92	73	78	80	87	94	96	101
58	70	74	77	83	89	92	96	77	81	84	91	98	101	105
59	73	78	80	87	94	96	101	80	85	88	95	102	105	110
60	76	80	83	90	97	100	104	84	89	92	100	108	111	116
61	79	84	87	94	101	104	109	89	94	97	105	113	116	121
62	83	88	92	99	106	110	115	92	98	101	109	117	120	126
63	88	93	96	104	112	115	120	97	103	106	115	124	127	133
64	90	96	99	107	115	118	124	99	105	108	117	126	129	135
65	95	100	104	112	120	124	129	103	109	113	122	131	135	141
66														
67														

Height in Inches	Fourteen years							Fifteen years						
	21.1 cm. 8.3 in.	22.3 8.8	23.1 9.1	24.9 9.8	26.7 10.5	27.5 10.8	28.7 cm. 11.3 in.	21.6 cm. 8.5 in.	22.9 9.0	23.6 9.3	25.4 10.0	27.2 10.7	27.9 11.0	29.2 cm. 11.5 in.
54	59	62	65	70	75	78	81	66	70	72	78	84	86	90
55	60	64	66	72	78	80	84	68	72	75	81	87	90	94
56	64	68	70	76	82	84	88	72	76	78	85	92	94	98
57	68	72	75	81	87	90	94	74	79	81	88	95	97	102
58	71	75	78	84	90	93	97	78	83	86	93	100	103	108
59	74	79	81	88	95	97	102	83	88	91	98	105	108	113
60	77	82	85	92	99	102	107	86	91	94	102	110	113	118
61	82	87	90	97	104	107	112	91	97	100	108	116	119	125
62	85	90	93	101	109	112	117	95	101	105	113	121	125	131
63	89	95	98	106	114	117	123	100	106	109	118	127	130	136
64	94	99	103	111	119	123	128	104	110	114	123	132	136	142
65	98	104	107	116	125	128	134	108	115	118	128	138	141	148
66	101	107	111	120	129	133	139	111	118	122	132	142	146	153
67	106	113	117	126	135	139	146	116	123	127	137	147	151	158
68	111	118	122	132	142	146	153	120	127	132	142	152	157	164
69	114	121	125	135	145	149	156	125	133	137	148	159	163	171
70	119	126	131	141	151	156	163	128	135	140	151	162	167	174
71	123	131	135	146	157	161	169	131	139	144	155	166	171	179
72								134	142	146	158	170	174	182
73														
74														

Height in Inches	Sixteen years						
	22.3 cm. 8.8 in.	23.6 9.3	24.4 9.6	26.2 10.3	28.0 11.0	28.8 11.3	30.0 cm. 11.8 in.
59	74	79	81	88	95	97	102
60	79	84	87	94	101	104	109
61	85	90	93	101	109	112	117
62	89	94	97	105	113	116	121
63	94	99	103	111	119	123	128
64	97	103	106	115	124	127	133
65	101	108	111	120	129	133	139
66	106	113	117	126	135	139	146
67	111	118	122	132	142	146	153
68	114	121	125	135	145	149	156
69	119	126	131	141	151	156	163
70	121	128	132	143	154	158	165
71	126	133	138	149	160	165	172
72	129	137	142	153	164	169	177
73	134	142	146	158	170	174	182
74	137	145	150	162	174	179	187

Directions: Take age at nearest birthday, and height at nearest inch. Measure the bi-iliac diameter and match it with the nearest diameter for the proper age shown along the top of the table. Appropriate weight for build is read for the given height at that width.

*Weight in pounds (without clothing).

The mean width-length index as calculated for each age sex group in our series was matched with the figures for the average height and average weight for each age sex group on the Baldwin-Wood table.* The 7 per cent underweight column from the Reference Table was matched with the figure for 7 per cent narrower than the mean of the width-length index for each age sex group; the 10 per cent underweight column was matched with the figure for 10 per cent narrower than the mean, and the 15 per cent underweight column was matched with the 15 per cent narrower than the mean of the width-length index. The over average weight columns were calculated in the same manner.

Since it seems cumbersome to print the width-length index with each weight the indices are omitted and only the width measurements are shown. The center width for each age and sex represents the mean of the measurements of the bi-iliac diameter for that age and sex in our series. The other widths are those from which the 7, 10, and 15 per cent variation indices were derived.

The Width-Weight tables offer seven normal weights for each height and age depending on the width of the iliac diameter. Since width measurements should be done next to the skin, the weights in the Baldwin-Wood table and from the American Child Health Underweight reference tables were corrected for clothes by subtracting one pound for heights 38 to 40 inches and two pounds for heights above 40 inches, as suggested in the Baldwin-Wood table. Our table is then a modification of the Baldwin-Wood table, taking width into consideration.

To use the Width-Weight table: age is taken at the nearest birthday and height at the nearest inch. The actual bi-iliac-diameter is matched with the nearest width measurement shown for the proper age sex group at the top of the table and the weight is read for the proper height at that width. Children who deviate very markedly from average; those too tall or too short, too broad or too narrow to be found on the table, should be considered individually.

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*In preparing Tables I and II, showing weight deviation in terms of width deviation, the regression formula: $y = (r_{xy}\frac{\sigma_y}{\sigma_x})x$ was applied as suggested by Dr. R. L. Jenkins. When x equals the percentage deviation from the mean width-length index for the age sex group and y equals the percentage deviation from average weight for height age and sex as given in the Baldwin-Wood table, application of the formula yields the following values:

	Ages	r_{xy}	$\frac{\sigma_y}{\sigma_x}$	
Male and Female	6, 7, 8, 9	0.48	2.19	1.051
Male	10, 11, 12	0.63	1.59	1.007
Female	10, 11, 12	0.622	1.45	0.902
Male	13, 14, 15, 16	0.46	1.85	0.951
Female	13, 14, 15, 16	0.51	2.05	1.045

It appears, then, that (within the limits of the tables presented in this paper) weight deviation varies in direct proportion to width deviation, since y equals approximately 1.

TABLE III

COMPARISON OF OLD AND NEW STANDARDS

SEX	AGE	PERCENTAGE DEVIATION FROM BALDWIN-WOOD WEIGHT				PERCENTAGE DEVIATION FROM WEIGHT FOR BUILD				TOTAL DEVIATION BALDWIN-WOOD WT.	TOTAL DEVIATION WT. FOR BUILD
		NO. CASES	AVER. PLUS DEV.	NO. CASES	AVER. MINUS DEV.	NO. CASES	AVER. PLUS DEV.	NO. CASES	AVER. MINUS DEV.		
M	4	6	11.7	4	7.7	5	7.9	6	5.1	+4.0	+2.8
F		2	10.8	2	6.0	3	9.8	1	5.0	+4.8	+4.8
M	5	3	11.9	3	8.4	4	7.2	2	10.1	+3.5	−2.9
F		7	11.7	13	10.4	7	6.9	13	8.8	+1.3	−1.9
M	6	7	8.7	22	8.7	7	7.9	21	6.4	0	+1.5
F		14	9.7	12	13.2	12	8.3	14	9.2	−3.5	−0.9
M	7	7	6.2	22	9.4	11	4.3	18	6.7	−3.2	−2.4
F		14	8.1	11	10.3	13	5.9	12	9.4	−2.2	−3.5
M	8	4	5.2	24	9.6	5	6.6	24	7.9	−4.4	−1.3
F		11	11.6	28	9.9	15	7.2	24	7.8	+1.7	−0.6
M	9	8	9.9	15	9.7	8	11.0	15	7.5	+0.2	+3.5
F		16	12.3	20	9.5	19	9.4	17	7.0	+2.8	+2.4
M	10	10	13.3	12	9.3	10	9.8	12	7.3	+4.0	+2.5
F		13	12.1	20	10.2	15	9.4	18	7.2	+1.9	+2.2
M	11	7	8.6	10	7.8	9	7.4	7	6.9	+0.8	+0.5
F		14	14.2	16	10.3	16	10.5	17	6.8	+3.9	+3.7
M	12	11	10.3	16	7.7	13	7.4	13	4.9	+2.6	+2.5
F		9	18.6	21	11.0	12	7.3	18	7.7	+7.6	−0.4
M	13	8	7.9	16	9.7	8	7.6	16	7.0	−1.8	+0.6
F		14	10.5	6	11.0	14	8.9	7	8.8	−0.5	+0.1
M	14	4	10.5	9	8.9	4	10.6	9	7.9	+1.6	+2.7
F		9	10.1	6	6.1	11	6.3	4	7.2	+4.0	−0.9
M	15	4	5.3	4	11.8	4	2.4	5	5.7	−6.5	−3.3
F		5	14.1	6	9.4	7	7.5	4	7.7	+4.7	−0.2
		207		318		232		297		71.5	48.1
		6 zero deviation 531 Cases Total				2 zero deviation				Total per cent deviation	

To test the superiority of the new width-weight tables over the original Baldwin-Wood tables the amount of deviation from each weight standard was measured on a series of 531 unselected healthy children. Table III shows the average amounts of deviation above and below the Baldwin-Wood normal and above and below the width-weight normal for each age and sex. Ages were distributed from four to fifteen years and deviations were measured in percentage of the normal.

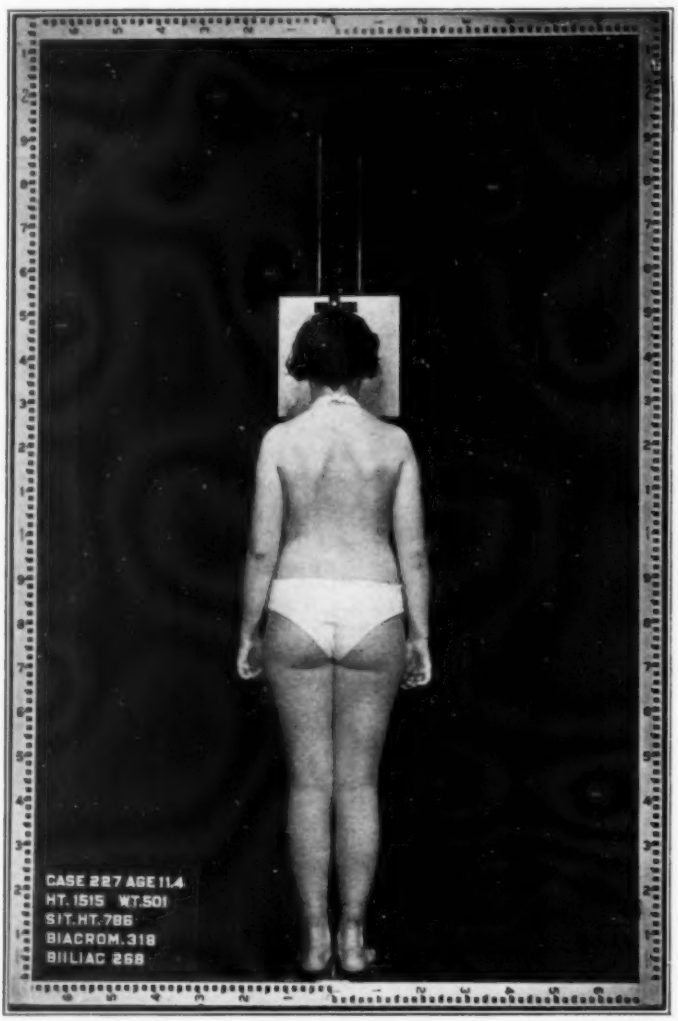

Fig. 3.—This girl is twenty-three per cent overweight by the standards of the Baldwin-Wood table, but since her width-height index is 10.7 per cent greater than the average for her age, her weight is only 12.3 per cent above the average for her age, height, and skeletal build. (The measurements shown on the photograph are in millimeters and hectograms.)

The total group of children vary from the new table 48.1 per cent (0.090 per cent per child) as compared with 71.5 per cent from the Baldwin-Wood (0.135 per cent per child).

For the general population as represented by the 531 unselected children the new width-weight table fits 32.7 per cent better than the Baldwin-Wood table.

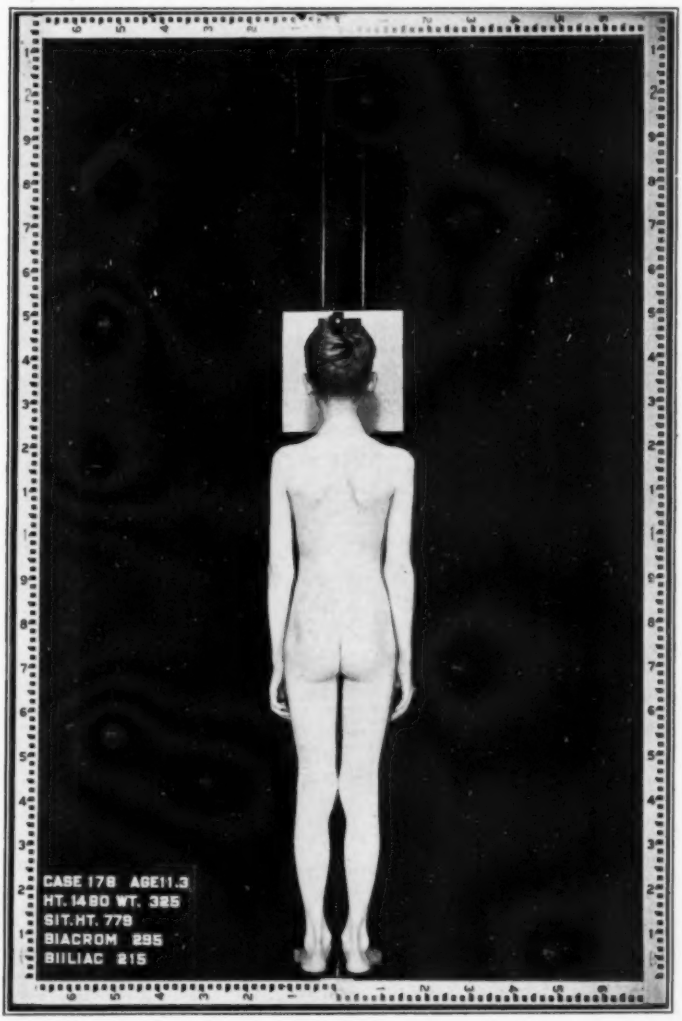

Fig. 4.—This boy is fifteen per cent underweight by the standards of the Baldwin-Wood table, but since his width-height index is 7.7 per cent less than the average for his age his weight is only 7.3 per cent below the average for his age, height, and skeletal build. (The measurements shown on the photograph are in millimeters and hectograms.)

TABLE IV

WIDTH-LENGTH INDICES

(Bi-iliac Diameter in Inches)

Height in Inches	17.7	18.3	19.0	19.6	20.3	20.9	21.6	22.1	22.9	23.4	24.1	24.6	25.4	25.9	26.7	27.2	27.9	28.5	29.2	29.7	30.5 cm.
	7.0	7.2	7.5	7.7	8.0	8.2	8.5	8.7	9.0	9.2	9.5	9.7	10.0	10.2	10.5	10.7	11.0	11.2	11.5	11.7	12.0 inches
44	161	165	170	174	181	187	192	196	203												
45	157	162	166	170	177	183	188	192	197												
46	154	158	162	167	173	179	184	188	195												
47	151	155	159	163	170	176	180	184	190	197											
48	148	152	156	160	166	172	176	180	186	193	197										
49	145	149	153	157	163	168	173	177	183	189	193	197									
50	142	146	150	154	159	165	169	173	179	185	189	193	199								
51	139	143	147	151	156	162	166	170	176	181	185	189	195	201							
52	136	140	144	148	153	159	163	167	172	178	182	186	191	197	201						
53	134	138	141	145	150	156	160	164	167	171	175	178	182	188	193	197					
54		135	139	142	148	153	157	161	166	172	175	179	184	190	193	197					
55			136	140	145	151	154	158	163	168	172	176	181	186	190	194	199				
56				137	143	148	151	155	160	165	169	173	178	183	187	190	195	197			
57				135	140	145	149	153	158	163	166	170	174	180	183	187	192	197	201		
58				133	137	143	146	150	154	160	163	167	171	177	180	184	189	194	197	201	
59					135	140	144	147	153	157	161	164	169	174	177	181	186	191	194	197	
60					135	138	141	145	149	155	158	161	166	171	174	178	183	187	191	194	199
61						136	139	142	148	152	155	159	163	168	173	176	180	184	188	191	196
62						133	137	140	145	149	152	156	160	165	168	171	177	181	184	187	192
63							134	138	142	147	150	153	158	163	166	169	174	178	181	184	190
64								135	140	145	148	151	156	160	163	166	171	175	178	182	186
65								133	138	142	145	148	154	158	161	164	169	173	176	179	183
66									135	140	143	146	150	155	158	161	166	170	173	176	180
67									134	138	141	144	149	153	156	159	164	168	171	174	178

TABLE V

MEAN WIDTH-LENGTH INDEXES FOR SCHOOL CHILDREN ARRANGED BY SEX AND AGE

Age in years	6	7	8	9	10	11	12	13	14	15	16
Index Boys	159	158	158	158	158	157	157	156	155	155	154
Girls	159	159	159	159	160	161	162	163	163	164	164

TABLE VI

PERCENTAGE DEVIATION CORRESPONDING TO EACH UNIT OF DEVIATION FROM THE MEAN WIDTH-LENGTH INDEX

WIDTH-LENGTH INDEX	PERCENT DEVIATIONS FROM AVERAGE INDEX FOR EACH UNIT OF DEVIATION									
	1	2	3	4	5	6	7	8	9	10
150-153	0.7	1.3	2.0	2.6	3.3	4.0	4.6	5.3	6.0	6.6
154-157	0.6	1.3	1.9	2.6	3.2	3.9	4.5	5.1	5.8	6.4
158-161	0.6	1.3	1.9	2.5	3.1	3.7	4.4	5.0	5.6	6.3
162-165	0.6	1.2	1.8	2.4	3.1	3.7	4.3	4.9	5.5	6.1
166-169	0.6	1.2	1.8	2.4	3.0	3.6	4.2	4.8	5.4	6.0
170-175	0.6	1.2	1.7	2.3	2.9	3.5	4.1	4.7	5.2	5.8

Example. The mean width-height index for eleven-year-old girls is 161. (See Table V.) For a girl of this age whose index is 166 the unit deviation is 5 and the percentage of deviation is 3.1 per cent. She is 3.1 per cent broader for her height than the average for girls of her age.

Table IV is included for the convenience of those who are interested in finding the width-length index. The bi-iliac diameter is found along the top and the standing height in the left-hand column. The width-length index appears where the two columns intersect.

Mean width-length indexes for our 4560 children by age and sex are shown in Table V. The width-length index for each child should be compared with the mean in this table; his percentage deviation may then be found by consulting Table VI. To use this device, determine the difference between the child's width-length index (found on Table IV) from the mean for his age and sex (found on Table V). Locate this difference along the top line of Table VI. Then find the mean width-length index for age and sex in the left-hand column of Table VI. The percentage deviation appears where the two columns intersect. This percentage deviation may be read as "8 per cent narrower than average or 12 per cent broader than average for age and sex." Since percentage deviation in weight from the Baldwin-Wood table allowed for body build is equal to the percentage deviation found on Table VI, the child who is 8 per cent narrower than average may weigh 8 per cent less than the weight assigned by the Baldwin-Wood table for his age and height. The child found to be 12 per cent broader than average may weigh 12 per cent more than the weight assigned on the Baldwin-Wood table.

In the rare cases where the percentage deviations from the width-length index are more than 15 per cent, an individual judgment should be made, although the principle of the relationship between width and weight is still applicable. If the table were extended to cover wider deviations from average, it would become too large and the chances

of inaccuracy would be greater since extreme deviations would be based on too few cases. The probability curve for deviation of normal persons from zero shows that there is one chance in about 150 of a deviation of 17 per cent and only one chance in about 500 of a deviation of 20 per cent.

SUMMARY

1. Nutritional status remains the best single criterion of health.

2. Relative width of the body, or body build, should be considered in judging appropriate weight for age and sex.

3. The relationship of body width to weight has been analyzed by mathematical correlation, using the measurements of 4560 school children.

4. A simple method of measuring body build has been used to help determine appropriate weight.

5. The four traits found to have the highest mathematical correlation with body weight are combined in new tables of appropriate weights for children aged six to sixteen years.

6. The new tables fit the general population much better than the Baldwin-Wood tables when deviations from both standards are compared for 531 children.

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HEREDITARY ATAXIA

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BROUSSEE gave the name of Friedreich's disease to the symptom complex described by the Heidelberg clinician in 1863.[1] This disease was characterized by onset during childhood, ataxia, loss of the patellar reflex, nystagmus, pes equinus, a slowly progressive course, and its occurrence in members of the same family.

The existence of this clinical picture was confirmed in a large number of publications, but it was soon found that the disease was not as sharply defined as at first described. Marie described a condition in young adults that had many points in common with the symptom complex of Friedreich, but differed in that there was a later onset, greater uncertainty in the gait, the tendon reflexes were present or exaggerated, there were ocular palsies, and occasionally atrophy of the optic nerve. The existence of this clinical picture was confirmed by a number of observers, and then cases were discovered combining symptoms of both diseases.

Most clinicians have come to the conclusion, in view of these facts, that Friedreich's disease and Marie's cerebellar ataxia can no longer be separated into two distinct groups either clinically or pathologically, and that it is more correct to include both of these conditions under the head of hereditary ataxia, with preponderance of the spinal symptoms in some cases and of the cerebellar symptoms in others.

The spinal form of hereditary ataxia appears in the first decade of life as a rule, while the cerebellar form shows the first symptoms usually after the age of twenty. However, there is no constant difference between the spinal and cerebellar forms as regards the age when the disease first makes its appearance. The outstanding symptom of the cerebellar form of hereditary ataxia is the uncertainty of the gait. The disturbance of coordination affects not only the walking, but also the standing and sitting postures. The motor unrest is not confined to the legs and early involves other portions of the body, producing wobbling of the head, tremor of the hands, and ataxia of the arms.

Peculiar postures of the feet are often found in the spinal form of hereditary ataxia. The malformations are caused by an over extension of the large toe, which may be an early symptom. As a rule, it is followed by a further malformation of the foot and clawlike position of the toes. Roentgenograms do not show anomalies of the skeleton.

It is interesting to note that as a rule either the male members or the female members of a family are exclusively attacked. However, there appears to be no difference between the sexes as regards frequency.

The behavior of the patellar reflex is not constant. As a rule, the patellar reflex disappears early in the spinal form of hereditary ataxia and is exaggerated in the cerebellar form, but there are spinal forms of the disease with exaggerated patellar reflexes and cerebellar forms of the disease with diminished reflexes.

When the spinal form of hereditary ataxia has existed for some time there is a scoliosis or kyphoscoliosis, due to the weakness of the spinal muscles.

A series of important cerebral symptoms frequently accompany hereditary ataxia. Nystagmus is common in the spinal form and occasionally absent in the cerebellar type. Disturbance of the ocular muscles, such as strabismus, ptosis, and diplopia, have been observed in the cerebellar type. Optic atrophy is frequently present. The pupils are normal.

Speech might be compared to the gait in that it is slow and sometimes scanning. The speech defect usually increases with the severity of the disease. The intellect is also impaired in the spinal form. There may be a few infrequent symptoms, such as profuse salivation and forced laughter.

It was formerly thought that in hereditary ataxia there were few if any sensory changes, but in the light of later case reports with anatomic studies this view has been changed.

The problem which the disease presents is not so much the distribution of the lesions with the resulting clinical picture as the causation and exact nature of the affection. The following case report is given and the literature briefly reviewed in order to help further determine, if possible, the nature of hereditary ataxia.

CASE REPORT

M. Y., white female child, three and a half years old, was born November 21, 1927. At this time her father was twenty-nine years of age and her mother twenty-five years of age. There were two older children, a girl of six years and a girl of two years, both apparently well. The mother had one miscarriage at four months between the first and second child.

The father's mother at the age of thirty-five developed an ataxia and eventually had to be placed in a hospital. The father died a few months after the patient was born.

The mother's health was good while she was carrying the patient. Birth was normal at full term, and the infant weighed nine pounds and twelve ounces. Feeding had to be supplementary.

At the age of five months the mother noticed that while the infant had developed remarkably well physically she could not hold her head up. Because the child was so chubby the mother thought she was just lazy. At six months the infant could hold her bottle. The child continued to gain but did not improve mentally. She was seen by several physicians who informed the mother that the child had a birth injury.

At the age of two and a half years the child was beginning to sit alone and could hold her bottle. She weighed 35 pounds. At this time she developed an acute illness with fever and an eruption which the mother says looked very much like

measles, but her doctor diagnosed as scarlet fever. She was quite ill at this time, lost much weight, and was very weak. She gradually recovered but it was now noticed that when the child reached for her bottle she would "grope," something that she had not done before. In addition it was noticed that she was "wobbly." Except for this one illness the child had been well.

There have been no inoculations or vaccination.

On physical examination the child was seen to be obviously defective mentally. She was quite chubby, her height was 35 inches and weight 38 pounds. The temperature was normal. The child would occasionally grimace, and roll her head to one side or the other. She would roll her body, and the spine was quite bowed. She was unable to walk.

Fig. 1.

The face showed but little expression. The hair showed nothing unusual, and the scalp was apparently normal.

The eyes showed no strabismus or nystagmus. She would follow her bottle and a light. The pupils were regular, equal, and reacted to light. Ophthalmoscopic examination showed a slight increase in paleness on the nasal side of the optic nerve.

The teeth and gums were normal.

The spine showed a kyphoscoliosis. There was considerable weakness of the spinal muscles.

The heart and lungs were normal.

The abdomen was rather flabby. The spleen and liver were not palpable.

The lower extremities showed a great deal of flabby tissue with poorly developed muscles. Motion was considerably restricted. When supported, the child kept the legs together though there was no abductor spasm. There was dorsiflexion of the large toes.

Fig. 2.

Fig. 3.

The child had fair use of the arms with marked ataxia and could hold her bottle. Muscle development was only fair.

The neurologic examination of the cranial nerves showed no abnormalities.

There was some weakness of the muscles of the trunk resulting in the kyphoscoliosis. The child could not crawl or walk and when sitting down was ataxic and would gradually roll over on her back to nurse her bottle.

The biceps, triceps, patellar, and ankle reflexes were hyperactive. Plantar stimulation gave dorsiflexion of the large toe.

Sensitivity was apparently normal.

The blood Wassermann was negative. Spinal puncture was not done.

PATHOLOGY

The changes in the posterior columns are the most definite and invariable features of hereditary ataxia, being essentially a systemic degeneration with neurogliar proliferation of the dorsal column. The disease process is not confined to the posterior columns but is more diffused with the causation quite obscure. The tracts most commonly involved are the crossed pyramidal tracts, the columns of Goll and Burdach, Gower's tract, the direct cerebellar tract, and, in some instances, Lissauer's tract and the column of Clark. In the upper part of the cord the degeneration, as a rule, is not so pronounced, but in the lumbar and sacral regions the degeneration involves almost completely the dorsal column.

A number of reported cases record no sensory disturbances. This paradox of preservation of sensation with pronounced degeneration of the posterior columns has been variously explained. Friedreich[1] said that the dorsal columns could not be the principal sensory tracts. Muller[2] came to the conclusion that the sensory impulses were conducted by naked axis cylinders within the degenerated tracts. Dejerine[3] thought that sensation was not affected by degeneration in the columns of Goll, and that alterations in the posterior columns may exist without sensory changes. Mott[4] claims that the neurones consisting of small cells and fine fibers which subserve cutaneous sensory and viscerovascular functions, are not affected in Friedreich's disease as in tabes dorsalis, and in consequence there are no visceral disturbances or loss of cutaneous sensibility. Pfeiffer[5] believes the characteristic sensory loss when found in Friedreich's ataxia is an essential rather than an exceptional feature in the symptomatology of the disease. He points out that when the forms of sensibility transmitted by the dorsal columns are impaired with only moderate ataxia, the degeneration affects principally the posterior tracts; but when sensory loss is slight in proportion to the ataxia, the spinocerebellar tracts are affected more intensely than the dorsal column tracts.

DISCUSSION

The causation of hereditary ataxia is obscure and has given rise to a variety of theories. The fact that it occurs in several children of

the same family at once suggests some obscure familial defect; but the additional fact that numerous brothers and sisters often escape indicates that the cause, whatever it is, is strangely limited or selective in its action. Gower's theory that the disease is due to an abiotrophy, or developmental defect, has been received with some favor.

Williamson[6] suggested that the location of the lesions in the posterolateral regions of the cord may be due to a less adequate blood supply, the supposition being that the local resistive power is less. These regions receive their blood supply from small meningeal branches instead of the deep central artery as in the anterior and central parts of the cord.

That the disease first makes its appearance with an acute infection is well recorded. Hess[7] reporting case histories of twin boys developing Friedreich's ataxia after an attack of influenza in 1918 raised the question as to whether he was dealing with boys with a normal mental and physical system who had undergone an acute infection of the nervous system resulting in degeneration and scoliosis, or whether the acute infection resulted in degenerations in congenitally defective nervous systems, and came to the conclusion that he was dealing with Friedreich's ataxia. Lloyd and Newcomer[8] report two children, of the same family and of the negro race, with indications of an unstable nervous system, the younger of whom developed ataxia at the age of six when he was recovering from typhoid fever. The development of ataxia in the present patient who obviously had a poor mental pattern was immediately preceded by an acute infection.

SUMMARY

A case of hereditary ataxia of the mixed type occurring after an acute infection in a white female child of two and a half years is reported.

The child in question had an obviously defective mental pattern.

CONCLUSION

Evidence is presented that given a congenitally defective nervous system in a child an acute infection can initiate a degenerative process of the dorsal columns of the spinal cord.

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VIRILISM AND HYPERTENSION IN INFANCY ASSOCIATED WITH ADRENAL TUMOR

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SCHENECTADY, N. Y.

VIRILISM associated with adrenal tumor has been frequently reported. Lesions of the pituitary may apparently produce a similar picture but Cushing's syndrome,[1] attributed to pituitary basophilism does not appear to include the changes in external genitals so striking in adrenal subjects and has been more often encountered in its extreme form in young adults. In an attempt to explain the similarity of signs produced by lesions of the anterior lobe of the pituitary and the suprarenal cortex, Langdon Brown[2] calls attention to the fact that both of these glands are in close association with nervous structures, the adrenal medulla being developed from sympathetic ganglion cells and the pituitary connected with the hypothalamus.

Renal hypernephroma, apparently more common in later life, is not believed to produce any alteration in sexual characteristics. A small number of malignant tumors of the ovary are accompanied by premature sexual development which, according to Frank,[3] must be ascribed to the influence of the ovarian growth because of the fact that recession of the prematurity takes place after the removal of the tumor; naturally no virilism would result. Pineal tumors, although they may cause sexual precosity and obesity, are not known to cause virilism. They apparently occur far more frequently in boys.

The case to be reported is unfortunately incomplete in that no autopsy was permitted and therefore no opportunity to examine the head postmortem; the very small sella turcica appearing in the x-ray film, however, strongly suggests the nonparticipation of the pituitary. The suprarenal factor was definitely demonstrated at operation, the manifestations being those expected from a suprarenal growth occurring in infancy: obesity, precocious development, hirsuties, voice change, virilism, and marked hypertrophy of the clitoris and external genitals together with hypertension and cardiac enlargement.

The infant, two years and two weeks old and of Italian parentage, entered the Pediatric Department of the Ellis Hospital on March 11, 1933. She was brought in by the parents, who feared a convulsion, with the history of having had convulsions "on and off" ever since birth. On the day of admission she had become very cyanotic. There is a very indefinite history of mild degrees of precocity in two related children, one a cousin. The father is exceptionally dark and virile in appearance, the mother, large, dark, and handsome rather than pretty.

Development was described as normal up to the end of the ninth month. She was mentally alert, sat up, walked, talked, and cut her teeth at the usual age periods

but at nine months she began to gain weight very rapidly and a dark growth of hair was noticed all over the body.

The infant was well supplied with subcutaneous fat, especially about breasts, shoulders, and face; her weight was 38½ pounds; her features were masculine, and

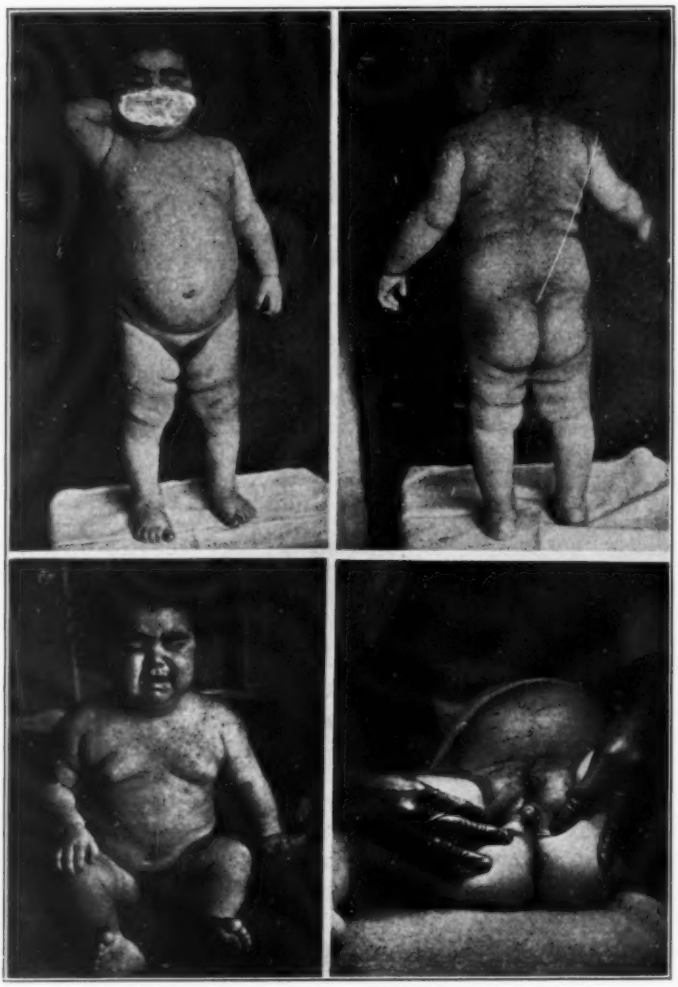

Fig. 1.—General appearance of child, showing growth of hair and enlarged clitoris.

she had a profuse growth of black hair on the back and pubic region, heavy eyebrows, and a rather definite mustache. The scalp hair was abnormally heavy and extended onto the face. Her dental formula was normal for her age. A papular rash and some pigmentation of skin were noted. Most striking was the development of external genitals: enormous hypertrophy of the clitoris, prominent vulvae, and a

dense growth of pubic hair, the vagina pervious and the urethra in the normal position in relation to vagina and clitoris.

Physical examination showed the heart evidently enlarged to the left and a mass could be felt in the right abdomen or at least a distinct difference in the two sides was evident upon percussion and palpation, although study of the abdomen was rendered exceedingly difficult by the obesity. Blood pressure registered 160/110 and the eyegrounds were reported as showing evidence of hypertension. Dr. Park, who made the ophthalmoscopic studies, reported tortuosity of the blood vessels, similar to that found in cases of high blood pressure, before learning of our pressure findings.

Fig. 2.—X-ray of skull, showing small sella turcica.

X-ray of the skull taken laterally showed nothing other than a sella turcica which appeared extremely small. This might be interpreted as indicating a small pituitary but it is only fair to note that the significance of this finding has been questioned. The thickness and contour of the cranium seemed normal for a child of that age. The heart shadow was extremely large, in keeping with the blood pressure and confirming the physical findings. A more than normal opacity in the right abdomen seemed to give additional confirmation to the diagnosis of right adrenal tumor. A ragged appearance of the lower epiphyses of the femora was demonstrated; haziness of the clinoid processes has been noted in two cases quoted by Langdon Brown as apparently due to deficiency of calcium salts. Several examinations of the urine

revealed only a large amount of amorphous material and a very faint trace of albumin; sugar was always absent, no blood was found, the number of leucocytes insignificant.

Blood Wassermann and Kahn tests were negative. Blood sugar 136 mg. per 100 c.c., possibly somewhat high, erythrocytes and hemoglobin low, with a leucocytosis of 24,000 two days before operation.

The patient was operated on the eighth day in the hospital by Dr. Stanton, and I quote from his record: Uterus apparently normal for age. Ovaries (estimated) 1 × 4 × 3 cm., equal in size. Both adrenals were large, the left smaller than the right which was adherent to the liver and measured approximately 9 by 6 by 7 centimeters, and so soft that it indicated malignancy; both were separate from the kidneys. The right adrenal was shelled out subcortically. Very little hemorrhage was reported at operation, although there was some oozing from the incision later. Death occurred within thirty-six hours.

No postmortem study was possible other than examination of the tumor mass by Dr. Ellis Kellert. Its weight was reported as 79.7 gm., the specimens consist-

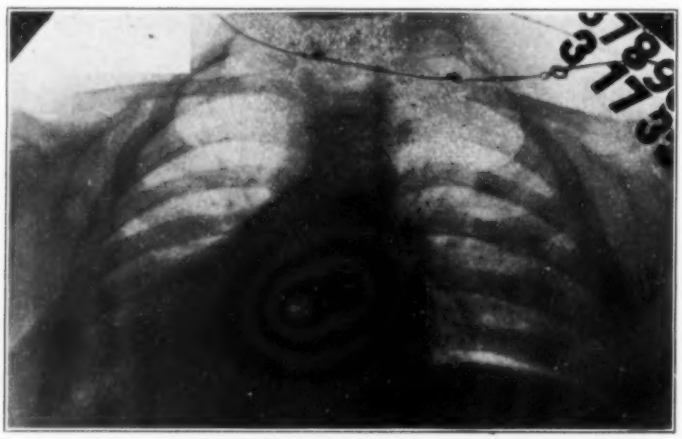

Fig. 3.—X-ray of chest, showing enlargement of heart.

ing of several masses of pale yellow, blood-stained, fatlike tissue, extremely ragged and irregular in shape, the largest piece measuring 6 by 4.5 by 3 cm. This piece, on section, was seen to consist of soft hemorrhagic tissue somewhat resembling dark red blood clot at the margins of which was soft, grayish tissue. Dr. Kellert reported that sections showed a cellular tumor together with extensive areas of necrotic tumor tissue and hemorrhage, the tumor cells large, poorly defined, and varying greatly in size. They appeared to be somewhat rounded and contained vacuolated cytoplasm. The nuclei varied greatly in size, many macronuclei and all stages of chromatic change being present. Certain cells contained several nuclei and others nuclear figures. The cells showed no definite arrangement but there was a slight tendency to grow in columns. Very little stroma was present. Anatomical diagnosis: Adrenal carcinoma.

The case is of the cortical type with definite, easily interpreted syndrome, although lesions of the pituitary and pineal must be excluded as causative factors. Tumors of medullary origin of the type first

described by Hutchinson produce only vague symptoms referable to the abdomen until the characteristic involvement of the skull occurs; their early diagnosis seems rarely possible although Peterman,[4] commenting upon a case of his own, states that tumors of the right suprarenal gland usually produce abdominal pain and thus direct attention to their presence.

In a recent number of the *Annals of Surgery*, Lehman,[5] of the University of Virginia, writes of a case of adrenal tumor removed from an infant of eleven months by Willard Bartlett of St. Louis. A description of this case was published in 1917 and commented upon as distinctive among undifferentiated tumors as the first case successfully operated upon. The child was alive and in perfect health fifteen years later. Collett's case,[6] operated upon in 1921 was, at that time believed to be the first to recover although recovery was not complete, all signs of virilism having not yet disappeared after two years. This case is especially interesting in that an indirect laryngoscopic examination revealed the vocal cords unusually long and broad, almost as in an adult male. Nine years later Harris and Plewes reported theirs as the second successful case.

Probably the youngest recorded case is that of Lightwood,[7] a male infant of eighteen weeks. The appearance of the baby was described as peculiar on account of the visible, hard deposits of fat in the cheeks and around shoulders and scapulae. There was a florid color of the face and the hair on the head was plentiful, with slight growth on the forehead but no development of hair elsewhere. A mass was felt in the left flank which appeared larger and lower than a normal left kidney. Pneumonia developed and death occurred eleven days after admission to the hospital. The tumor was demonstrated at autopsy.

In the last few years the results of surgical removal have been most encouraging, though certainly dependent, in malignancy, upon early recognition before metastasis has occurred. Cecil's recent statistics,[8] show that all the cases that had cortical hyperplasia and adenoma, excepting where congenital, recovered from the operation and also were cured of the disease with loss of abnormal distribution of hair and fat and recession of the clitoris to normal. Twenty-two per cent of the patients with hypernephroma completely recovered. Since most of the fatalities occurred within a few hours after operation, a technic designed to prevent shock is essential. Cecil advises tying of the vessels, particularly the veins, before manipulating the tumor, to obviate the danger of metastases of detached particles and to prevent a large amount of secretion from being suddenly squeezed into the circulation. It is imperative to know that the corresponding gland is functioning.

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THE TREATMENT OF PERTUSSIS WITH GOLD TRIBROMIDE

Report of Seventy-Five Cases

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PERTUSSIS is one of the common communicable diseases of childhood, affecting all races in all climates. It varies greatly in its epidemiology, virulence, and seasonal prevalence. Since the disease is universal and there is only a slight natural immunity to it, the number of whooping cough cases must be very large. The death rate from whooping cough per 100,000 population in the registration area in the United States for the last thirty years averages 9.92. The younger the child, the greater the mortality. The number of children in the United States dying from pertussis and its complications is estimated to be about 25,000 a year.

History.—In all probability, whooping cough was known to the early Greek, Roman, and Arabian physicians and to the physicians of the middle ages. The first epidemic of pertussis occurred in Paris in 1578 and was described by Ballonius. The second epidemic occurred in London in 1658 and was recorded by Thomas Willis. Sydenham described the disease more fully in 1670 and again in 1679. Pertussis appeared in Germany in epidemic form in 1724. During a general epidemic which spread throughout Europe in 1732, the disease was carried to America.

Etiology.—An organism of the influenza group which is known as the *Bacillus pertussis* or the Bordet-Gengou bacillus has been generally accepted as the etiologic agent of whooping cough. A great deal of doubt has recently been cast on the etiologic relationship of this organism to pertussis. Much research work is in progress on the etiology of whooping cough and some filtrable virus may be found to be the real cause of this universal disease.

Anatomic and Physiologic Pathology.—The chief anatomic pathologic condition in pertussis is a catarrhal inflammation of the upper respiratory tract with degeneration of the ciliated epithelium. The mucous membrane secretes a thick, whitish, tenacious substance consisting chiefly of mucus, epithelial cells, leucocytes, and microorganisms. The submucosa is swollen and edematous and there is, in many cases, a peribronchitis with a peribronchiolitis. There may be other pathologic conditions affecting various organs as a result of the toxemia or the physical violence due to the stress and strain of coughing. The physiologic pathology is characterized by a hyperirritability of the cough center. The toxemia of whooping cough lowers the threshold of the cough

center so that the slightest central or peripheral irritation causes a shower of coughing spasms. The proximity of the coughing center to the respiratory and the vomiting centers accounts for the respiratory distress and the frequent vomiting in pertussis.

Diagnosis.—In the majority of cases, there is no difficulty in making a correct clinical diagnosis of pertussis. A bacteriologic, hematologic, or serologic diagnosis is of value in doubtful cases. A history of exposure to the disease, a persistent paroxysmal cough with a tendency to be worse at night, a negative finding on physical examination, and an apparently well child between the paroxysms are indicative of whooping cough.

TREATMENT

During the middle ages, and even up to the seventeenth century, whooping cough was treated with irrational folk-remedies. Later, various herbs were highly recommended. At the present time, a large number of drugs are being used with poor therapeutic results. Vaccines have been used for some years with gradually diminishing enthusiasm. Convalescent blood serum has been tried and discarded. Ether, given intramuscularly or by rectum, has been in vogue for some time, but has proved of little value and much discomfort. X-ray treatments over the chests of whooping cough patients have been tried but have not gained much therapeutic popularity. Carbon dioxide inhalation was recently suggested but its practical application is difficult in general everyday practice.

In an effort to find some reliable medicine for the treatment of pertussis, I began several years ago the study of the therapeutic effect of the anti-whooping cough drugs in common use. I divided them as nearly as possible, into hypnotics, sedatives, and antispasmodics and gave each group a careful and thorough trial in a fairly large number of cases. The results were not encouraging. I then made a special study of the bromides and classified them into monobromides or univalents, dibromides or bivalents, and tribromides or trivalents. Potassium bromide (KBr), sodium bromide (NaBr), lithium bromide (LiBr), and ammonium bromide (NH_4Br) are univalent bromides. Calcium bromide ($CaBr_2$) and strontium bromide ($SrBr_2$) are bivalent bromides. Gold bromide ($AuBr_3$), iron bromide ($FeBr_3$ or Fe_2Br_6), arsenic bromide ($AsBr_3$), and aluminum bromide ($AlBr_3$) are trivalent bromides. In observing the action of the bromides, I found that the dibromides gave better sedative or bromine action than the monobromides and the tribromides were more effective than the monobromides or the dibromides. Of the tribromides, the most suitable preparation for medicinal purposes is gold tribromide. This drug I have used in whooping cough for the last four years with satisfactory results.

In the therapeutic study of gold in whooping cough, I used the neutral salt of gold tribromide. This is a compound of gold and hydrobromic acid which has no free acid. It is brownish black in color, deliquescent and soluble in water. Its gold content is about 45 per cent. This chemical is to be distinguished from acid bromauric, N. F., which is an acid salt of gold and hydrobromic acid with some free acid. It is reddish brown, unstable, very deliquescent, and freely soluble in water. It contains about 32 per cent of gold.

The pharmacologic action and the therapeutic effect of gold tribromide in pertussis is probably due to a specific chemical reaction between the gold and the tribromine ions, with the formation of a compound which has neurosedative, antispasmodic, and antibacterial action. The compound of gold tribromide reduces the reflex irritability of the cough center and causes general sedative and antispasmodic effect. It shortens the period of the illness, diminishes the number and severity of the paroxysms, and prevents complications.

Treatment consisted in the administration by mouth of a solution of gold tribromide in water. The dosage varied with the age of the child and the severity of the paroxysmal cough. As a general rule, $\frac{1}{20}$ to $\frac{1}{10}$ of a grain, three times a day after meals and once at midnight was given. It was found, however, that a solution of gold tribromide in water did not keep well on standing for some time. There were frequently some slight chemical changes with a sedimentation, due probably to oxidation. To avoid using an unstable medication, I am now prescribing a uniform, stable, palpable preparation known as Elixir gold tribromide (Elixir bromaurate).* The dosage is a teaspoonful three or four times a day after meals.

Result of Treatment.—The result of treatment in 75 whooping cough cases during the last four years was most encouraging. Of the 75 patients, there were 43 females and 32 males, the ages ranging from two weeks to eight years. There were 2 adult cases. In about two-thirds of the whooping cough patients, the cough subsided in three weeks; in the others, it abated within from five to seven weeks. In all cases, after three or four days' treatment with gold tribromide, the cough was less frequent and less distressing, the attacks were shorter and milder, the vomiting ceased, and the sleep was more restful. There were no recurrences, complications, or fatalities in this series of cases. In 25 controls who received the usual antipertussis remedies, the cough was frequent and racking and the course of the disease was long, varying from three to four months.

Postural Treatment.—It is well known that the cough in pertussis is worse at night. In fact, this has been accepted as one of the symptoms of pertussis. The reason for the incessant coughing at night has

*Elixir Gold Tribromide (Elixir Bromourate) may be obtained from Schieffelin & Co., New York City.

never been made clear. It occurred to me that this was due to an over-stimulation, during sleep, of the cough center which is hypersensitive in pertussis. In the recumbent, sleeping position, the lungs do not expand fully and there is a decrease in oxygen and an increase in the carbon dioxide of the blood. This increased concentration of the carbon dioxide in the blood causes an over-activity of the hyperirritable cough center giving rise to the distressing paroxysms at night. To overcome this most annoying condition, I have whooping cough children sleep in a semi-reclining position. When propped up in bed, there is a better ventilation of the lungs with freer respiration, more oxygen inhalation, less carbon dioxide concentration and less stimulation of the cough center. This simple postural treatment is giving whooping cough children considerable rest at night.

SUMMARY

Whooping cough is a serious disease in its mortality rate, complications, and sequelae. It affects all races in all climates. It is essentially a disease of childhood. The etiology of pertussis is still not definitely established. The anatomic pathology shows an inflammation and degeneration of the upper respiratory tract. Physiologically, there is a hyperirritability of the coughing reflex arc which responds to the slightest physical or psychic stimuli. Most of the treatments recommended for whooping cough are either ineffectual or not practical of application. As a result of a study of many drugs, especially the bromides, in the treatment of whooping cough, gold tribromide is seemingly an effective remedy in a large number of cases. The earlier in the disease the treatment is begun, the quicker and better the results. The compound of gold tribromide inhibits the coughing reflex arc, allays the general nervous irritability and relieves the spasmodic attacks which cause damage to every system of the body.

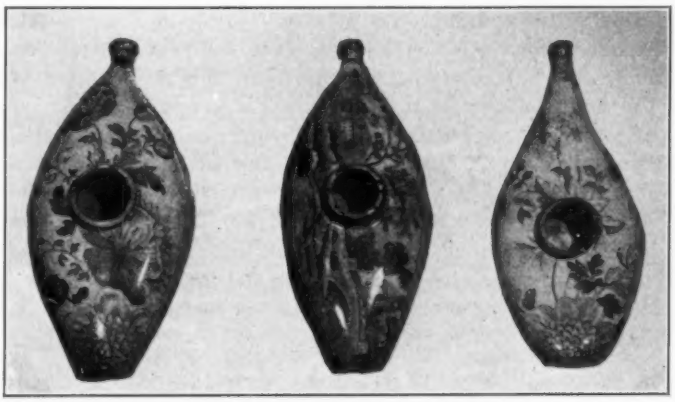
222 East Eighty-second Street.

ANTIQUES OF PEDIATRIC INTEREST

T. G. H. Drake, M.B., F.R.C.P.(C)

AS EARLY as 1686 pottery works had been established in Staffordshire where clay and coal were easily obtainable.

Josiah Spode, the founder of the Spode firm, was originally apprenticed to Thomas Whieldon, where he worked with Josiah Wedgwood. In 1770, he bought the pottery works of Banks and Turner at Stoke and in 1797 was succeeded by Josiah the second, during whose period William Copeland was taken into the firm. Josiah the third died in 1829. In 1833 Thomas Garrett joined the firm, and until his retirement in 1847 the firm was known as Copeland and Garrett late Spode.



Spode Staffordshire transfer printed pottery feeding bottles (length 7 inches).

Marks: Left and right, Copeland and Garrett late Spode, circa 1833; center, Copeland late Spode, circa 1847.

Since that time the style has been Copeland late Spode. The many productions associated with this famous factory are still perpetuated by Messrs. W. T. Copeland and Sons.

In 1780, Thomas Minton engraved his famous willow pattern, evolving and arranging his design from several different Chinese sources. Originally there were only two figures on the bridge, no flying doves and no conventionalized cedar. The pattern was an immediate success, different versions were engraved with additions from other Chinese originals, and finally the pattern as we now know it was evolved. From the final composition has grown up the legend of

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the love of a daughter of a Chinese mandarin for her father's secretary and the punishment by imprisonment of the daughter by her father who had intended her for an old but wealthy suitor; of the escape of the lovers to the cottage by the sea where the life honeymoon was to be spent, the burning of the cottage by the disappointed suitor, and the transformation of the lovers by the Immortal Gods into two doves.

Transfer printing of pottery was introduced into Staffordshire by Josiah Spode in 1784 with the old willow pattern. Later other blue printed designs were used.

Transfer printing is a method of printing on a rigid or uneven surface by means of paper prints applied to the ware. It was probably used first by the Battersea Enamel Works about 1750. Somewhat later its use in decorating pottery was discovered independently by Sadler of Liverpool, who with Green was so successful in this method of decoration that pottery was sent to them from all parts of the country for printing.

In transfer printing a metal plate, usually copper, is engraved in the usual way but somewhat deeper than for printing on paper since the firing of the pottery reduces the strength of the colors. The color is then rubbed into the lines of the warmed plate, the superfluous pigment is scraped off and the surface is wiped clean with a pad. A print is taken on damped tissue paper and this is applied to the ware and carefully rubbed into contact. The piece is next immersed in water, which removes the paper and leaves the print unharmed since the pigment is mixed with linseed oil. The piece is then fired over or underglazed as the case may be.

Critical Review

TUBERCULOSIS IN CHILDREN

LEE FORREST HILL, M.D., DES MOINES, IOWA

IN THE Critical Review of the October, 1932, issue of THE JOURNAL OF PEDIATRICS, the attempt was made to sum up the prevailing views on tuberculosis in children. This discussion is intended as a continuation of that report and is based on the literature of the past year.

The National Tuberculosis Association[1] has published a second brochure entitled *Childhood Type of Tuberculosis, Diagnostic Aids,* with chapters by Opie, Aronson, McPhedran, and Chadwick. It has received the approval of the Committee on Childhood Tuberculosis of the American Sanatorium Association and is to be highly recommended to those who wish a clear and concise presentation of the subject in condensed form.

Dr. J. A. Myers[2] has also published a second book called *The Child and the Tuberculosis Problem* which not only sums up in detail the present conceptions of the subject but also contains many advanced ideas which he has acquired as a result of his extensive studies at Lymanhurst during the past decade.

The set-up at Lymanhurst has embodied an unusual opportunity for a follow-up study of a large number of tuberculous children over a period of ten years. The results of this ten-year period of study have been published by Dr. Myers, chief of staff, and by Dr. Chester Stewart, pediatrician on the staff, in a number of articles. Their observations have forced them to conclusions that, in many instances, are in direct conflict with beliefs generally held, but which on the whole have tended to simplify and clarify the whole picture. In the pages that follow, the opinions of these authors have been freely set forth, for the purpose of bringing out fully these new concepts established by them.

TERMINOLOGY AND CLASSIFICATION

Some controversy exists in the literature as to the classification of the various types of lesions occurring in children as the result of first infection by the tubercle bacillus. The brochure referred to above states that "The childhood type of tuberculosis is the name adopted by the National Tuberculosis Association to describe the diffuse or circumscribed lesions in the lungs and associated tracheobronchial lymph nodes resulting from a first infection of the pulmonary tissue with the tubercle bacillus. It is recommended that this term, 'childhood type of tuberculosis,' be used instead of 'infantile,' 'juvenile,' or 'hilum tuberculosis.' It specifically includes lesions of the tracheobronchial lymph nodes. The childhood type of tuberculosis is usually found in children. It infrequently occurs in white adults but is not uncommon in adult negroes, Mexicans, American Indians, Porto Ricans, and Filipinos."

In a subsequent chapter McPhedran classifies the lesions of childhood type tuberculosis on the basis of x-ray observations as follows: "A. Focal tuberculosis; caseous or calcied nodule. B. Tuberculous consolidation of a lobe or wedge, progressive or unstable; calcified spots remain if it clears. C. Tuberculous consolidation of a lobe or wedge, retrogressive and benign. Few strands remain when it clears. D. Diffuse, childhood type tuberculous infiltration. Confluent bronchopneumonia is the serious lesion of this type and often precedes E. E. Miliary tuberculosis. F. Tuberculosis of tracheobronchial lymph nodes, uncalcified. G. Tuberculosis of tracheobronchial lymph nodes, calcified."

Myers[3] states that their present classification consists of:

1. Negative to tuberculosis. In this group are placed those children who are negative to the tuberculin test when a full milligram of tuberculin has been administered intracutaneously, and who have no other abnormal findings due to tuberculosis.

2. Primary tuberculous infection. This group consists of those children who react positively to the tuberculin test but in whom no evidence of tuberculous disease can be obtained by x-ray, physical, or laboratory examinations.

3. Childhood type of tuberculosis. In this group the children react positively to the tuberculin test and in addition have some evidence, usually by x-ray, of the location of the focus or the foci. The lesion may be represented by a shadow indicating an inflammatory process which is progressing, stationary, or receding, or it may be represented by shadows indicating deposits of calcium. These lesions need not necessarily be in the chest. When evidence of calcium deposits is found in lymph nodes anywhere, particularly in the cervical region or in the mesentery, the classification is that of childhood or first infection type of tuberculosis. Further subdivided into:

(a) Those with the inflammatory stage when first seen, progressing, stationary or receding.

(b) Consists of those lesions in which deposits of calcium can be demonstrated by x-ray examination.

4. Adult type of tuberculosis. In this group have been placed all of the definite clinical forms of tuberculosis whether the lesions appear in the lungs, bony framework, or elsewhere.

Myers expresses dissatisfaction with his second group. He feels that a sharp line should not divide cases with demonstrable lesions from those without demonstrable lesions when a positive tuberculin test is present in both groups. He believes it is erroneous to attempt to distinguish between tuberculous infection and tuberculous disease. A positive tuberculin test means a focus of tuberculous disease somewhere within the body, and only the pathologist has the right to say whether it is "healed" or not.

Stewart[4] in a more recent article expresses his belief that the terminology and classification set forth in the previously mentioned brochure should be revised in order that it be more in keeping with the known facts concerning first infection with the tubercle bacillus. The term "childhood type tuberculosis" as now defined limits itself to include lesions occurring only in the lungs and tracheobronchial lymph nodes. Since the primary focus or foci of infection may be extrapulmonary, and since the childhood type of tuberculosis does occur

in adults, Stewart feels that the terms "first infection types of tuberculosis" or "primary tuberculosis" would be more appropriate. Furthermore he objects to the term "adult tuberculosis" on the basis that this lesion does occur in children with appreciable frequency. He prefers that these lesions be designated by the term "reinfection type of pulmonary tuberculosis."

He is not satisfied with a classification based upon appearance of lesions in the x-ray films of chests. Compared to the tuberculin test and pathologic examination, the x-ray is a relatively crude screen since in only about 25 per cent of first infection cases does the x-ray reveal lesions with sufficient clearness to be identified as such. Ghon[5] in his well-known pathologic studies was able to demonstrate a tuberculous focus in 90 to 95 per cent of positive tuberculin reactors. Both Stewart and Myers express their conviction that a positive tuberculin test specifically indicates a tuberculous focus somewhere within the body, but our present methods of examination during life are inadequate to demonstrate such foci in at least half the children.

Stewart further states that, "no evidence is found in the follow-up observations made during the past decade at Lymanhurst to indicate that cases presenting single or multiple, large, partially or heavily calcified scars show a definitely greater tendency to manifest symptoms of impairment in health referable to primary tuberculosis, or to suffer a different ultimate fate, than do infected children who have small or no lesions demonstrable during life. As far as I have been able to ascertain, all cases of primary tuberculosis are basically identical except that a few cases (from 3 to 4 per cent of infected children) with acute diffuse primary tuberculous pulmonary infiltrations exhibit symptoms which on this basis temporarily distinguish them for a time from the general group of infected cases. After these acute manifestations subside, patients with first infection types of tuberculosis are clinically indistinguishable from one another as a rule, and remain so until the day arrives when reinfections transfer a certain percentage of them to the consumptive group."

A classification proposed by Stewart outlines roughly the stages of evolution of tuberculosis as it occurs in man. The first group constitutes the general population. A second uninfected group is identified by negative tuberculin reactions. The third group is the primary tuberculosis group or first infection types of tuberculosis, or "patients whose bodies harbor foci of tuberculosis of first infection (identified by positive tuberculin reaction). [This group includes 'first infection pulmonary' (childhood type by definition in the brochures); retroperitoneal, or cervical lymph node tuberculosis)]. Note may be made in these cases relative to the appearance of lesions found, but assumptions that visualized conditions provide reliable evidence that these cases differ basically and require grouping separate from others in the general first infection group apparently are unwarranted." The fourth group contains first infection types of tuberculosis with symptoms. Only 3 or 4 per cent of infected children are in this group and their sojourn here is temporary. The fifth group is comprised of first infection types of tuberculosis without symptoms definitely referable to their disease. The majority of cases fall in this group. The sixth group is designated as the secondary tuberculosis group or first infection types that later develop reinfection types of tuberculosis (consumption, and the like). The final group is the primary tubercu-

losis group or first infection types of tuberculosis that do not develop reinfection types of tuberculosis.

Washburn[6] feels that on the basis of newer knowledge secured by tuberculin, x-ray, and pathologic studies the terms the "pretuberculous" or "potentially" tuberculous child, "latent" or "suspected" tuberculosis are of doubtful value as diagnoses. The attempt to distinguish between "tuberculous infection" and tuberculosis he thinks is also of dubious significance, and the term "tuberculosis of childhood type" may be misleading. He prefers the classification as proposed by Ranke[7] in 1916 in which the disease process is divided into three stages; a primary phase of invasion, a secondary phase of spread to lymph nodes associated with the development of an allergic response, and a tertiary phase which represents actual visceral involvement. The first two stages commonly occur in childhood and the third in adult life, but all three may be found in infancy. This is essentially the view of the German School as set forth in the *Handbuch der Kindertuberkulose* for 1930 by Herbert Koch, Epstein, Engle, Priesel, Zarfl, Liebermeister, Weise, and others, as referred to by Collis and Brookington.[8]

Blau and Rosenbaum[9] feel it is a misnomer to designate the primary complex of Ranke as childhood tuberculosis. This latter term "should be limited to cases in which a definite and distinct parenchymatous involvement is depicted by the x-ray, with a positive Mantoux test, and with more or less distinct clinical manifestations, simulating in a measure pulmonary tuberculosis in the adult." They feel the pulmonary tracheobronchial gland lesions defined in the brochure as childhood type tuberculosis should be designated by the term "primary pulmonary tuberculous complex."

It is apparent, therefore, that there is still lacking by a wide margin a uniform opinion in the interpretation, terminology, and classification of lesions produced in the human body by the initial infection with tubercle bacilli.

LESIONS

From studies, such as those which have been carried on at Lymanhurst and elsewhere, sufficient data have been collected to give the physician some idea of what he may expect in the way of x-ray findings in his positive tuberculin reacting children. Roughly speaking, at least half of the positive reactors will have negative films, 25 per cent will show questionable or doubtful lesions, and the remaining 25 per cent will show definite lesions characteristic of the childhood type of tuberculosis.

In the 50 or more per cent of positive reactors who give negative roentgenologic findings, the primary focus may be assumed to be extrapulmonary, too small to cast a shadow, or obscured by other structures. Except for this difference of visualization, or failure of visualization of lesions, it probably should be emphasized that symptomless positive reacting children are in all essential respects to be regarded alike so far as their tuberculous experience is concerned.

In the 25 per cent of films revealing definite lesions, it may be expected that the parenchymal lesions will be found more often in infancy and early childhood, the calcifications in middle and late childhood, and the adult type of tuberculosis in the teen age.

Myers[3] reports his x-ray findings in 4,737 positive tuberculin reactors as follows: Questionable calcification in hilum, 4.12 per cent; slight, moderate, and marked calcification in hilum, 9.35 per cent; Ghon tubercles, 6.04 per cent; questionable Ghon tubercles, 0.8 per cent; calcification hilum, fibrosis extending into lung parenchyma, 0.55 per cent; childhood type tuberculosis in lung parenchyma (inflammatory stage), 0.87 per cent; marked enlargement hilum, without calcification, 0.38 per cent; marked enlargement hilum infiltration extending to parenchyma, 0.8 per cent; total positive findings, 22.91 per cent; adult type tuberculosis, 1.28 per cent.

Stewart[10] in a group of 579 positive reactors found the following lesions revealed by the x-ray: Resolving parenchymal [comparable to childhood type tuberculosis in lung parenchyma (inflammatory stage) of Myers], 4.7 per cent; questionable calcification, 8.6 per cent; slight calcification, 13.8 per cent; moderate calcification, 5.2 per cent; marked calcification, 2.2 per cent; Ghon tubercles, 11.6 per cent; adult type tuberculosis, 2.2 per cent.

RESOLVING PULMONARY LESIONS

Some further discussion of the lesion referred to above by Myers as the childhood type tuberculosis in lung parenchyma (inflammatory stage), and by Stewart as resolving parenchymal pulmonary tuberculosis, seems warranted. It is probable that this is the same lesion referred to by Eliasberg and Neuland, Goldberg and Gasul, and others, as "epituberculosis" and in all probability, in the past the terms "splenopneumonia," "gelatinous pneumonia," "perifocal inflammation," "circumfocal inflammation," "paratuberculosis," "perituberculous inflammation," and "collateral inflammatory edema" were all used to designate this same type of lesion. In common with all descriptions, has been the basic fact of a more or less massive, slowly resolving pulmonary shadow, characterized by paucity of physical signs and symptoms occurring in children who have positive tuberculin reactions. According to Stewart[10] such lesions represent the earliest stage of the primary pulmonary infection. Up to date he has observed seventy-three such cases. Two of these have been under observation for nine months, a third for twenty-eight months, and the remaining sixty-eight cases for periods ranging from three to nine years. No deaths have occurred. He states that "In most cases (all in our experience) extensive parenchymal lesions resolve and disappear leaving relatively inconspicuous calcified scars and, during the months this resolution is taking place, the patient, whether a young infant or an older child, may enjoy excellent health. At times severe and alarming symptoms are present for variable periods early in the course of the disease, following which a long period of symptomless convalescence ensues."

Martin[11] in California presents a series of sixty cases that she has seen. She divides them into three groups on the basis of variation in physical signs and symptoms rather than on any fundamental pathologic differences. All the children had positive tuberculin tests. Sixty-five per cent had a history of contact. Eighty per cent of the children were under six years of age. All had pulmonary infiltrations of varying degrees of massiveness as revealed by the x-ray. Twenty-nine were acutely ill, with physical signs of consolidation. Eighteen of the sixty were ailing but had slight or absent physical findings. Thirteen were apparently healthy children with practically negative symptoms

and physical findings. Four of the series died. Three of these were in the acutely ill group and were seriously ill when first seen; the other death, due to tuberculous meningitis, was in the second group. In the remainder, the parenchymal lesion gradually resolved leaving either an area of calcification or cleared completely. Atelectasis of a lobe was present in three cases. Evidence of enlarged tracheobronchial lymph nodes in association with the pulmonary infiltrations was present in 45 per cent of the series. Martin does not feel the presence of these enlarged glands added greatly to the gravity of the prognosis. She concludes that "acute tuberculous pneumonias are more frequent than is generally recognized. They have a good prognosis if seen early, and if repeated infection is prevented by separation of the child from the source of infection."

Bruce[12] also discusses this lesion and the favorable prognosis of primary tuberculosis in general, and presents films of four cases of pulmonary tuberculosis which he has seen undergo satisfactory resolution.

Reichle,[13] in a most interesting article, discusses the mechanism of resolving exudates in tuberculous children. He regards the observations of the authors who first called attention to these massive lobar shadows as being of crucial importance. However, he believes that up to the present time there is no unanimity of opinion concerning the nature of such lesions. Atelectasis, secondary pyogenic infection in tuberculous tissue, and lymphatic congestion have been suggested as mechanisms. The majority, however, look upon these exudates as being areas of inflammation about tuberculous tissue, the inflammation being due to a "poison" from the destroyed tissue or a "toxin from the tubercle bacillus in the focus of 'true' tuberculous inflammation." The rôle played by allergy in the production of these resolving or "fugitive" exudates is discussed by the author. He states that "allergy is probably an essential condition of a fugitive exudate." To quote further, "The primary infection occurs in virgin soil; the tissue is not specifically sensitized to the tubercle bacillus and its chemical constituents. This is probably the reason for the minuteness of the lesion, the slight surrounding inflammation, and the ultimate state of characteristic morphology. Never again can the body react to the tubercle bacillus in this fashion; every subsequent defense will be conducted with a striking increase in the auxiliary phenomena of peripheral vascular dilation and extravasation of the cellular and amorphous material which constitutes an inflammatory exudate. The second characteristic of hypersensitive tissue is its tendency to undergo the type of necrosis known as caseation." He feels that the majority of the lesions under discussion are tuberculous pneumonias which have failed to go on to caseation; some may be atelectases, and some lobar or bronchopneumonias. He disagrees with Stewart's idea that these resolving lesions are restricted to the stage of the primary infection. He concludes that "since resolution is possible in almost every form of tuberculous inflammation, there is no reason for [redacted] on any unusual mechanism to explain the retrogressive tuberculous exudates."

H. C. Cameron[14] describes a case of apparent resolving parenchymal tuberculosis which cleared rapidly leaving a small focus. He concludes "that the existence of benign infiltration remains to be proved. It can only be demonstrated by the accident of an opportunity being afforded to perform an autopsy during the time when the extensive consolidation is present."

Whether the lesion which has been referred to by such a galaxy of terms has some unusual pathogenesis uncommon in tuberculosis knowledge, or whether, as Stewart suggests, it merely represents the usual course of events in primary infections, is probably still an open question. However, the increasing frequency with which resolving lesions are being reported coincident with the increasing use of tuberculin and x-ray suggests that in the past they have gone unrecognized, and to this extent lend support to Stewart's idea.

IMMUNITY

Perhaps one of the most revolutionary ideas that has developed as a result of the study of tuberculosis in large numbers of children by means of tuberculin and x-ray is that a primary infection does not confer protection against phthisis. In other words, a positive tuberculin test in a child can no longer be held to be an advantage, as an indicator of immunity. Nor can it be held to be a liability to reach adult age with a negative test. Myers[3] has observed nurses on tuberculosis wards, who, at the beginning of their services reacted negatively to tuberculin, but who later developed positive tests. X-ray pictures of their chests have shown lesions similar to the primary type of infection seen in children. In no instance has he seen "galloping consumption" occur in adults who had grown up with a negative test, as was once supposed to be the fate in store for such unfortunates if they chanced to acquire tuberculosis.

If our former ideas are correct, one would not expect to see adult type tuberculosis developing in healthy children with positive tuberculin tests showing evidences of primary tuberculosis only. Stewart,[4] however, in reporting his observations on 10,000 children at Lymanhurst in the last ten years found eighty-four cases of phthisis, thirty-six of whom had had primary tuberculosis exclusively for varying periods up to ten years and then developed the reinfection type of pulmonary tuberculosis. Twenty-five of the eighty-four children had primary and reinfection pulmonary tuberculosis coexisting when first examined. Thus sixty-one, or 73 per cent of these eighty-four children with phthisis presented unmistakable evidence that their primary infections did not prevent them from developing the serious and fatal form of adult, or reinfection type tuberculosis. Insufficient data were available on the remaining twenty-three children to provide evidence for or against the question under discussion. Opie, at the autopsy table, found lesions of primary tuberculosis in all cases of reinfection type or adult type of tuberculosis. It would seem, therefore, on the basis of such evidence as presented above, that the allergic state does not imply protection, and the necessity of preventing continued exposure to tubercle bacilli, whether it be the infant with his primary infection just beginning, or the older child with his calcification well established, far overshadows all other considerations combined in the treatment and prevention of tuberculosis in children.

PROGNOSIS

The opportunity of watching a comparatively large number of primary pulmonary infiltrations resolve and finally end in the production of Gohn tubercles or other calcifications, has led Stewart[15] to the belief that infants and children seldom, if ever, succumb to a single primary infection. He believes an individual can resolve a primary infection

to the calcified stage once and only once. In no instance has he observed a subsequent repetition of this process in the same child, nor has he observed a case of phthisis which has developed as a direct result of a first infection. Repeated reinfections may, of course, overcome the natural powers of resistance of the child and result in fatal generalized or reinfection types of tuberculosis. In the days before the use of tuberculin and serial x-ray films, it was only cases of this latter type that were recognized, and the natural assumption was that tuberculosis in early life was an extremely serious disease. That such an outcome, however, is the exception rather than the rule, and that children are endowed to cope with reasonable doses of tubercle bacilli, on the whole, equally well, if not better than adults, is one of the remarkable changes in thought being brought about by these newer methods of study. The almost universal good health found in the group of children with primary infections, the majority of whom are unaware of their tuberculosis, or when it started, has led to the logical conclusion that first infection type of tuberculosis is a benign form of the disease, in contrast to reinfection types which are progressive and tend to be fatal.

TREATMENT

Both Myers[3] and Stewart[16] have pointed out the conclusions they have reached in regard to the treatment of primary tuberculosis. The one essential is that opportunity for reinfections must be prevented. For this reason, and because of the uniformly favorable outlook in this type of the disease, they believe sanatorium care, even with massive resolving pulmonary lesions, is undesirable and unnecessary. Well managed homes, or foster homes free from tuberculosis, provide all that is necessary in the treatment of such patients without adding the risk of reinfection, which is a possibility in the hospital ward or sanatorium.

Children who develop the adult type of tuberculosis need sanatorium care. Myers[3] agrees with Chadwick that collapse therapy for these cases is indicated much more frequently than has been the custom in the past.

EVOLUTION OF TUBERCULOSIS

By way of summary of what has been said heretofore, the following outline, representing Stewart's[10] conception of the evolution of tuberculosis in the human lung, is presented.

1. Primary tuberculous infections of the lungs are revealed by the roentgen ray films as parenchymal infiltrations, calcified glands, and Ghon tubercles.

2. These lesions, although varied in appearance, merely represent different stages in the development of one and the same clinical condition; namely, primary tuberculosis, or tuberculosis of the childhood type.

3. The general tendency for lesions resulting from an initial infection by the tubercle bacillus is first to resolve and later to calcify.

4. The human body can resolve a tuberculous infection into what is known as the primary complex only once.

5. When once reduced to calcified scars, these primary tuberculous lesions do not become reactivated later in the production of the adult type of tuberculosis (consumption).

6. Death seldom, and possibly never, results from a single primary pulmonary tuberculous infection. The prognosis is excellent in infancy as well as in later childhood, provided reinfection is prevented.

7. Primary tuberculous infections of the lung, if extensive, produce symptoms of varying severity, which subside in the course of a few to several weeks. Thereafter, throughout the remainder of the life of the patient, these primary lesions produce no clinical symptoms. (Occasionally a very large Ghon tubercle acting as a foreign body may erode a blood vessel and cause hemotysis, and in rare instances may be expelled from the lung in coughing.)

8. Consumption (phthisis) does not develop as a result of an initial infection by the tubercle bacillus. The first infection occurring at any age in life uniformly resolves and calcifies.

9. Consumption develops following a reinfection of individuals who previously have had a primary infection.

10. The reinfections responsible for the development of phthisis are probably exogenous in origin in the majority of cases.

11. The lesions of reinfection (adult type of tuberculosis or phthisis) usually appear in the subapical portions of the lungs.

12. These lesions may be present for months and years, without producing symptoms, physical findings or showing any tendency to spread.

13. During the teens, previously dormant lesions characteristic of the adult type of tuberculosis frequently tend to spread, produce cavities and cause death.

14. The adult type of tuberculosis seldom calcifies.

15. Puberty seems to favor the breaking down of previously existing, apparently quiescent, subapical infiltrations of the adult type of tuberculosis. Primary infections occurring during puberty, however, behave much the same as similar infections taking place in infancy and early childhood.

16. Lesions of the adult type of tuberculosis tend to spread and cavitate, whereas, infiltrations resulting from initial tuberculous infections tend to recede and calcify.

17. The prognosis is grave for the adult type of tuberculosis. This type of the disease frequently results in death, whereas, primary infections are seldom fatal.

18. The relationship existing between the childhood and the adult type of tuberculosis seems to consist largely in the tendency for the primary infection to prepare the patient for the development of phthisis, should he perchance later experience a reinfection of sufficient severity to produce an intrapulmonary lesion.

19. Phthisis apparently does not ordinarily result from a lighting-up of an old infection received in childhood.

20. The part the former childhood infection seems to play in favoring the later development of phthisis depends more upon the changes which this primary infection caused with respect to the manner in which the body reacts thereafter to the tubercle bacillus and its products, rather than upon a lighting-up of the old disease acquired during childhood.

MODERN CASE FINDING

One of the most important recent developments in the public health phase of tuberculosis work is area testing, or case finding. The object is to search out the spreaders of tubercle bacilli and find infected children before they have developed serious tuberculous disease. Proper disposition of these two groups is, of course, the final goal.

The success achieved by the veterinarians in stamping out the disease among cattle is an example and a challenge to the workers among human beings.. "In certain parts of the United States," says Stewart,[17] "certified areas exist in which no cow is in danger of contracting tuberculosis from other members of the herd, and in these certified districts to be a calf is safer than to be a baby, in so far as tuberculous infection is concerned." And again Myers[2] remarks that some herds of cattle are in greater danger from human sources of tuberculous infection than from bovine sources.

So long as the opinion was held that tuberculosis was practically universal after the age of ten, tuberculin testing had a very limited field of usefulness, but when area testing of children showed a variation of positive reactors from 10 per cent in some rural communitits, to as high as 75 per cent in certain sections of large cities, with an average among large groups of children of around 28 per cent, the possibilities of a tremendously increased field of usefulness of diagnostic tuberculin in screening out the infected from the uninfected became apparent.

The x-ray, too, must be given its full share of credit for the new vista which has opened up in the control of the great "white plague." An x-ray film of every positive reactor is now considered an essential. Amberson, Barnard, and Loew[18] conducted an experiment with paper films and conclude that while they are not quite as clear as celluloid films, they are satisfactory for most diagnostic work, and that the disadvantage is offset by the greatly increased number of films that may be taken with no increase in expense.

Also, the clearer realization that as a contagious disease, tuberculosis presents an epidemiologic problem not dissimilar in many respects to that of typhoid fever or diphtheria, has brought out the possibilities of public health regulations for the control of this disease that may in time be equally effective with those in force for the control of other contagious diseases. It is interesting to note that Geer[19] has instituted a medical aseptic technic in the tuberculosis division of the Ancker Hospital in St. Paul. From 1928-1930 an incidence of tuberculous disease of 5.5 per cent developed among the nurses of the training school. From 1931, when the new technic went into effect, up to the present time, the incidence of tuberculous disease has been only 1.6 per cent, which compares favorably with that found among the nurses of five other general hospitals.

How long it will take for area testing of children to become as general over the country as testing of cattle now is can only be surmised. Already many states have begun in earnest to attack the problem. Massachusetts with its ten-year program, and 100,000 children tested in the first five years, is the outstanding example. Tennessee, as reported by Bishop and Stewart,[20] five years ago embarked on a state wide program for control of tuberculosis with "the central and dominating idea behind this program to bring about finding of every case of tuberculosis as early as possible and placing all

cases found under adequate medical and nursing care." They conclude that "The logical means of approach in the control of tuberculosis in Tennessee, in the light of information now at hand, would seem to center around the breaking of the chain of long-continued contact between patients with fibroid and other types of tuberculosis with their household associates. Eventually this would mean the establishment of hospitals or retreats for the care of the patient who is spreading tuberculous infection among members of the family and friends."

In Minnesota, Anderson[21] reports the results of tuberculin testing surveys carried on by ten county tuberculosis sanatoria. These ten institutions tested a total of 23,424 children of whom 16.76 per cent were positive; 89.16 per cent of the positive reactors were x-rayed; 10 per cent showed evidence of childhood tuberculosis and 2 per cent adult tuberculosis. "The goal of these sanatoria," says Anderson, "is, year by year to come closer to an 'accredited' group of school children."

Surveys have been carried on in Delaware by Phillips,[22] and by Sargent[23]; in Texas by Gray,[24] and by Sellers[25]; in Colorado by Einhorn[26]; and in Yonkers, New York, by Littell.[27] Brachman[28] gives the results of case finding in three high schools in Detroit. He says that "The Detroit Tuberculosis Society's custom, of giving health certificates to high school graduates on physical examination, will in the future include tuberculin testing and x-raying of the reactors."

Leggett and Myers[29] studied the incidence of tuberculous infection among the high school students of Morrison County, Minn. Three hundred seventy-six tests were made, with 14.9 per cent positive reactions.

Hewitt and Cutts[30] tested 1,328 high school students in Rochester, Minn., and found 11.5 per cent reacting positively. Of thirty-four students definitely known to have been exposed to open tuberculosis, 61.8 per cent were positive; 15.1 per cent of the positive reactors had x-ray lesions suggestive of tuberculous infection.

Soper and Wilson[31] made stereoscopic films of all the entering classes (1,644 entrants) at Yale University in 1930 and found thirty, or 1.8 per cent, showed evidence of pulmonary tuberculosis, and 229, or 14.4 per cent, showed calcifications designating the childhood type. In 1931, tuberculin tests were made on the 1,502 entrants; 59.7 per cent gave a positive reaction. The reactors were examined under the fluoroscope, and any showing a suspicious shadow were x-rayed. Thirteen were found to have pulmonary tuberculosis. From this study the authors conclude that fluoroscopy as a method is not sufficiently accurate. The method to be used in 1932 will be a single film of all entering students. They point out the superiority of routine roentgenography of students' chests in detecting tuberculosis, over the method of physical examination alone used in the decade previous to the present study.

Myers and Wulff[32] give their observations on tuberculosis in students at the University of Minnesota for the last eleven years. Since 1928, tuberculin testing has been routine on all entering classes. About one-third of the students react positively. The cost has prohibited x-raying all the positive reactors but many have been done at the students' expense. Since 1929, routine x-raying of the entering classes to the School of Nursing and School of Medicine has been practiced. Each year a new film has been made so that senior students will have been x-rayed at least four times. It is hoped to extend this service to

all classes in the near future. By this method it has been possible to determine almost exactly when infection has occurred in these two precarious professions, and to trace the source of infection with considerably less difficulty.

Prior to 1928, the method of finding cases of tuberculosis among the students was to wait for them to present themselves for examination because of illness. Several cases are cited to show the faults of this latter plan. Frequently the disease had progressed to such a far advanced stage when the diagnosis had been made on physical signs and symptoms that death or very serious illness was the inevitable result. Furthermore, such individuals were frequently spreaders of tubercle bacilli among their fellow students on the campus. In the future, it is the plan at the University of Minnesota to test all entering students with tuberculin, x-ray the positive reactors, and repeat the testing on all negative reactors at intervals throughout the university course.

Other surveys have been reported, particularly among the Indians in the Midwest and Northwest, and among the Orientals, but perhaps the above citations are sufficient to show that a real beginning has been made with modern weapons in a direct attack upon the strongholds of tuberculous disease. It is certainly to be hoped that other states will realize the value of this splendid work, and embark upon programs that have as a goal the eradication of tuberculosis within their borders.

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THIRD ANNUAL MEETING OF THE AMERICAN ACADEMY OF PEDIATRICS

MONDAY AFTERNOON SESSION
June 12, 1933

Round Table Conference on Rheumatic Heart Disease in Children

The meeting was called to order at 2:15 P.M. in the Berwyn Room of the Edgewater Beach Hotel by the Chairman, Dr. Hugh McCulloch, St. Louis, Mo.

DR. HUGH McCULLOCH.—This conference on rheumatic heart disease is to follow the one held last year under the direction of Dr. Morse. The general subject of rheumatic infection was covered by him and many important questions relating to diseases of the heart were presented. In order to continue the discussion, it has been deemed wise to present four principal articles and to limit discussion to these. I have therefore selected four separate articles, each of which is somewhat different and yet all are related.

First: A definition of what the rheumatic state or rheumatism means:

An antigen (toxin) formed by recurring infection in one or more areas of the body (sore throat, common colds) and operating in an injured host (malnutrition) produces fixed (proliferative) and/or wandering (exudative) tissue response in the various susceptible parts of the body.

a. Tonsillitis/nasopharyngitis (sore throats, colds).
b. Arthritis (joint pains).
c. Carditis—myo-, endo-, peri- (heart disease).
d. Encephalitis (chorea).
e. Nephritis.
f. Pneumonitis.
g. Peritonitis.

The second article for discussion would be the factors which influence the manifestation of rheumatic fever and heart disease in children.

1. Type of response shown by the patient.
   a. Sensitized individual (exudative).
   b. Desensitized individual (proliferative, hyperplastic, aplastic).
   c. Nonsensitized individual.
2. Age when the first attack occurs.
   a. Progressive and recessive growth of tissue.
3. Race.
4. Climate.
5. Social status.

The third article is the care of children who have rheumatic heart disease.

1. During the period of active infection.
   a. Evidence; active focal infection, fever, rheumatic nodules.
   b. Treatment; clean out foci of infection. Salicylates, rest. Congestive failure.
2. During the period of convalescence.
   a. When does it begin? Normal temperature and pulse rate. Good appetite, no fatigue.
   b. Criteria of satisfactory progress: Gain in body weight and height to expected normal. Freedom from infection.
3. During the period of quiescence.
   a. Avoid infection by contact.
   b. Daily routine, balance of activity and rest.
   c. School and/or work. Desirable. Fitting for life work. Learn limitations.
   d. General health. Food calories, variety, vitamins, fluid. Sunlight, fresh air. Quiet, sleep.
4. The time when they become healed, or we think they are cured.
   a. Prognosis. Myocarditis. Endocarditis (aortic and mitral). Pericarditis.
   b. Probable chance of recurrence.

The fourth article is the discussion of the relation of rheumatic fever and heart disease in children to heart disease in adult life.

1. Healed juvenile types in adult life; aortic and mitral; chronic cardiac valvular disease.
2. Subacute bacterial (streptococcus) endocarditis in old congenital or acquired heart disease.
3. Myocardial failure after an old myocardial injury from rheumatic fever, scarlet fever, pneumonia, influenza, diphtheria, syphilis.
4. Coronary heart disease.

The presentation of the first two subjects will be taken up, followed by a discussion, before proceeding with Articles 3 and 4.

Definition of Rheumatic Infections.—It is very apparent that "rheumatic infections" is an inclusive term used to cover many manifestations of the rheumatic state in different individuals. For many years the term "rheumatism" was used to define those conditions associated with painful swelling and structural changes in joints, as well as certain other symptoms and signs more or less related to the joints. Following this early use, there occurred a period when an attempt was made to differentiate more clearly the various lesions occurring in rheumatism, and there has been a tendency to differentiate these diseases too sharply and to do away with the older term. Since rheumatic infection in children is a process involving many parts of the body in different ways and at the same or at different times, it may be advisable to again use a single term, "rheumatism" or "rheumatic infection" or the "rheumatic state" to include these various protean manifestations. Since heart disease is such a constant and important manifestation of rheumatism in children, it may be advisable also to include "rheumatic heart disease" as a general term of the same sort as the others. The decision as to which term is best will probably rest with common usage and not come about by any special edict or order.

The following definition of the rheumatic state is now proposed for discussion: "An antigen (toxin) formed by recurring infection in one or more areas of the body (sore throat and common colds) and operating in an injured host (malnutrition) produces fixed (proliferative) and/or wandering (exudative) tissue response in various susceptible parts of the body."

The nature of the antigen producing the changes in the body is not yet certain. Investigative work done so far indicates that this substance is not of the nature of a filtrable virus, though this possibility cannot be finally dismissed. Recent studies on the virus of the "common cold" reported by Dochez may have some bearing on a virus of a similar sort being the antigen of rheumatic fever. The experimental evidence suggests that it is a bacterial product of the general order of toxins formed by streptococci growing in some focus, usually in the nose and throat area. Specificity for either the toxin itself formed by the organisms or for the organisms themselves has not been proved. Indeed, the more recent bacteriologic studies of Swift and others seem to indicate that many organisms may be responsible at times, or that one organism may liberate different toxins at times.

The nature of the infection which liberates the antigen varies a great deal; it may be a single infection in the tonsils or recurring infections of varying severity in the nose and throat area, or it may be located in other parts of the body. The tonsils, the nasopharyngeal mucous membrane and the sinuses, however, seem to be the usual areas involved. This infection may manifest itself in different ways, either as sore throats, common colds, coryzas and tonsillitis.

Malnutrition must play an important part in determining the incidence of rheumatic infections as well as their manifestations in a given child. Malnutrition manifests itself in children in many ways, all of which are more or less familiar to us and need not be discussed fully at the present time. It has been our observation in a large group of cardiac children that most of them give a history during infancy and childhood of improper feeding, housing, general care, and of recurring infections of the type usually considered to be associated with a low body resistance and malnutrition. How important this association may be is difficult to prove. Its high incidence, however, suggests a probable close relationship. The usual conception of malnutrition in children is that of underweight and undernutrition with a low body resistance to infection. It should be pointed out, however, that quite frequently children may be obese and suffer equally from malnutrition and low body resistance to infection. We have observed this type of malnutrition very frequently in children with chorea.

The nature of the manifestations of the rheumatic state in children varies, and may be of two general types. First, a response on the part of the fixed tissue elements of the body, producing structural changes in the various parts of the body, particularly the heart. These have been classified by Swift as proliferative changes. The essential process is the formation of rheumatic nodules (Aschoff bodies), together with changes in the heart muscle, in the valves and the pericardium. These lesions occur also in other parts of the body, particularly in the brain and lungs. The second type of response is due to changes in the wandering tissue elements of the body, characterized principally by acute transient exudative processes such as leucocytosis, fever, edema, etc., in joints, heart structure, brain or skin. While these two types can be well defined and frequently children may be seen who belong entirely to one or the other type, there may be children who show signs belonging to both types, who, therefore, are mixed. The exact clinical differentiation at times, therefore, may be difficult.

While manifestations of the rheumatic state occur in many parts of the body, there are certain principal locations where it is usual to find either or both, proliferative and exudative changes.

a. The tonsillitis and/or nasopharyngitis is regarded as the initiating cause of an attack of rheumatic fever and serves as the focus of infection from which the antigen is liberated. It also seems probable that the inflammatory changes in the tonsils and/or nasopharynx may be a manifestation of the rheumatism itself. Full

discussion and investigation is very much in order on this point. It may be pointed out that a child who suffers from rheumatism should be seen by the attending physician during the time when the acute process in the nose and throat area is going on, in order to determine the appearance of the lesion then, as well as in the interim between attacks. It is only in this way that a proper classification of this process can be made.

b. Painful joints are a common manifestation of rheumatism from which the condition derives its important terminology. When true joint pains occur in children, they are usually due to rheumatism, and except for the occasional small child who has a "septic" arthritis, rheumatism should be suspected in all who complain of joint pains. Opinion today definitely excludes growing pains as a manifestation of rheumatism; indeed, there should be serious question as to whether pain can result from growth in any way. Its further use should be discouraged. The most important pain in the extremities occurring in children not due to rheumatism, is that which results from fatigue. In our opinion, this type of pain is very common and simulates closely that of rheumatism. It usually occurs at night after going to bed, is usually in the lower extremities and is not associated with other signs of rheumatism. It is described by the child as a soreness in the legs and does not occur in the region of the joints. In such children flat feet must be considered also.

c. The manifestations of rheumatism in the heart are so well known that they need not be discussed here. Suffice it to say, the three important regions of the heart are usually involved and in a child who has repeated attacks of rheumatic fever, one may safely assume that the endocardium and the myocardium are always involved, and that sooner or later the pericardium will show changes. The term carditis is used frequently by pediatricians to indicate the widespread changes occurring in the hearts of these children. Endocarditis should mean rheumatic heart disease with endocarditis.

d. Chorea is frequently found in connection with rheumatic manifestations and more and more is being looked on as a specific type of encephalitis due to the action of the toxin in the brain, particularly in the lower basal nuclei. These changes in the brain usually are of the exudative type, though occasionally rheumatic nodules and proliferative changes may be found.

e. The relationship between inflammatory changes in the kidney due to infection and rheumatism is not so clear. It has been our observation that children with rheumatic heart disease show some form of nephritis more frequently than a normal group, and it also is well known that children with nephritis resulting from infection in the nose and throat frequently may have important structural changes in the heart. When these changes occur, they are of the type usually found in acute rheumatic fever. The relationship may not be close, but there are certainly many similar points. Children with nephritis do not show rheumatic nodules in the kidney tissue, though the "crescent" changes in the glomeruli may at times simulate this same process.

f. In the last ten years pathologists have pointed out lesions in the lungs and pleura which probably are of a rheumatic nature. Structures resembling Aschoff bodies have been found and the interstitial change in the lungs and pleura bears many resemblances to the lesions in the heart muscle and endocardium. Von Glahn and Pappenheimer have pointed out the probability that pneumonitis and pleuritis of this type may be a manifestation of rheumatic fever.

g. Certain cases of peritonitis have been reported in which it seems probable that the lesion was due to rheumatism. These case reports so far have not been frequent, though it is quite possible that many of them have either been overlooked or have not been investigated with the idea of a possible relation to rheumatic infection. This point can be carefully investigated when suspicious cases occur.

Factors Influencing the Incidence and Manifestation of Rheumatic Fever and Heart Disease in Children.

1. It has been pointed out by Swift that the nature of the rheumatic infection varies with the type of response shown by the patient to the infection. In individuals who have been sensitized previously to streptococcic infection, particularly adults, an attack of rheumatic fever manifests itself principally by exudative signs, especially painful joints, with redness and swelling, fever, leucocytosis, prostration, and by acute myocarditis, endocarditis and pericarditis. It is also known that such an individual tends to show well-defined attacks of rheumatic fever with a period relatively free from activity in between. These cyclic attacks are not seen commonly in children. It also has been shown that individuals who have been sensitized to streptococcic infection, probably will show proliferative changes of a hyperplastic type, especially rheumatic nodules, Aschoff bodies, chronic or subacute myocardial, pericardial and endocardial changes and pneumonitis. This type of response can be reproduced satisfactorily in laboratory animals. In the non-sensitized individual, the proliferative response is usually aplastic in nature and not associated with the formation of rheumatic nodules and Aschoff bodies, but with a progressive injury described by Swift as a "cachectic" or "anergic" type. It is this type which we have seen frequently in very young children during the first attack of rheumatic fever, and with a fatal termination.

2. The age of the patient when the first attack of rheumatism occurs apparently determines to a considerable extent the manifestations of rheumatic fever. During childhood the process is apt to be widespread throughout the body as well as involving all parts of the heart. It also is during this period that the joint pains are less severe and less constant and in early childhood, particularly under the age of two, joint pains rarely occur. During adult life the joint pains occupy a much more prominent part of the picture of rheumatism and the disease is more localized in any tissue. It is also well known that the chance for the heart to be involved during adult life is much less than during childhood. It is interesting to note that certain adults may show the same form of rheumatism seen during childhood. It is probable that these individuals have never had an attack of rheumatic fever or an infection of this type previous to the onset of the disease. We have had opportunity to observe on several occasions, children who have shown attacks of rheumatic fever similar to that seen more frequently during adult life. These children in each instance have shown other signs of biological maturity and growth, so as to make it seem probable that the nature of their rheumatic attack was determined by an early maturity. This difference in age periods needs further study and clarification. It is suggested that the important subject of the nature of growth may determine itself the type of response shown by the patient. It is quite possible that during the period when progressive growth is taking place; i.e., an increase in number, size and function of cells, the manifestations of the disease will be influenced to a considerable extent by this factor. Likewise, during the period of life when recessive growth is occurring; i.e., decrease in size, number and function of body cells, other manifestations may present themselves because of the different type of growth process. It must be pointed out in this connection that the human body shows both types of growth at any given period of life; that while progressive growth predominates during childhood, there are certain recessive changes taking place also and likewise during adult life after maturity, recessive growth predominates, there may be certain progressive changes occurring simultaneously. This important subject needs investigation in the light of more recent studies on the nature of growth.

3. The influence of race on the manifestation of rheumatic fever has been considered for many years, and recently important information has been developed on this point. While certain races seem to show a lower incidence of the disease,

it seems more probable that this is due to a difference in location rather than a difference in race. Recently Porto Ricans living in New York City have been found to show a high incidence of rheumatic fever, whereas when living in their native state, the disease tends to be rare. A group of New York children with rheumatic heart disease, including several Porto Ricans, were transplanted to Porto Rico for a year, and during this period the signs of rheumatism disappeared. When these individuals returned to New York City, the disease reappeared. Such studies tend to show that race is less of a factor than location.

4. The question of climate as a factor in the incidence of the disease has also been considered for a long time, and at present is not solved. Rheumatic fever with heart disease is found more frequently in the north temperate zone throughout all parts of the world than in any other location. There is also an opinion that the disease is found infrequently in the southern parts of the United States, in the tropics and in similar climatic zones in the southern hemisphere. The disease is not frequent among the Chinese living in the north temperate zone nor is it frequent in South America and Africa. The few observations made in these remote parts of the world, however, do not entirely settle this important question and further study is needed.

5. The social status of patients with rheumatic fever is generally low, and in a recent report from Dr. Paul from New Haven it was shown that the disease occurred more frequently among Yale University students who had come from a lower social status. A definite opinion on this general subject, however, is not available and certainly it warrants further study. It is probable that important secondary factors enter largely into the high incidence of the disease in the lower social strata; for example, bad housing, frequent infections, close contact with bacterial carriers and improper care during minor illnesses, particularly ordinary colds. The importance of these secondary factors in the higher incidence of tuberculosis is well recognized and they probably play an equally important part in the higher incidence of rheumatic heart disease.

This covers the first two articles of the outline, and Dr. Bachmann will introduce the discussion.

DR. HARROLD A. BACHMANN (CHICAGO).—I have not attempted to agree or to disagree with the things Dr. McCulloch has said in his paper, but as I read it over I felt there were certain clinical factors which it might be well to review.

Dr. McCulloch's paper is so clearly conceived and so thoroughly logical that it is difficult to know where to begin this discussion. Of one thing I am sure, that in the main most of us agree with the statements he has made, and few will take serious issue with the conclusions he has drawn. In regard to the usage of rheumatism in our terminology, I feel strongly that it should be retained. If nothing more, it conveys to the laymen a striking symptom which should be urgently impressed upon them at all times. Our success in this field of cardiac disease in children still lies in its prevention, and without descriptive terminology we cannot attempt to accomplish our purpose.

It would seem to me, in spite of the completeness of Dr. McCulloch's definition of the rheumatic state, that there should be added some statement to the effect that the culmination of the entire rheumatic picture is definitely associated with environmental, climatic and hereditary factors. Without these, the rheumatic state, one might say, could not and does not exist.

I feel that one point further should be made regarding the rheumatic infection —once it has been inflicted upon a child we should never consider it as cured, but rather, as in tuberculosis, consider it quiescent, or as an "arrest of the process."

The broader view regarding the etiologic factors, as expressed by Swift, is highly commendable. It logically explains the bacterial differences of the past, and presents a working basis with which to start.

I am fully in accord with the opinion that malnutrition is an important contributing factor in the production of rheumatic infections. The question that comes to mind, however, is, should we stop here? I am convinced that there are contingent factors of environment which are equally important. Many of these have been strongly emphasized in the current literature. The contagious factor, and the indulgent care of the parents to minor infections should receive additional consideration and discussion.

In regard to the manifestations of the rheumatic state I feel that tonsillitis should be further qualified. Among ourselves and certain economic groups, it may be well to emphasize tonsillitis in relation to rheumatic heart disease. With the average private practice group this emphasis should be guarded. People are so health conscious these days that it behooves us to be careful not to add another worry to the now anxious pseudoscientific mother.

In considering joint and muscle pains I am sure we are all convinced of the importance of any arthritis symptoms in childhood. I do feel that every joint pain should be considered rheumatic unless otherwise proved. I wonder, however, whether one should assume a totally benign attitude toward growing pains. Fatigue, as stated, is a rational explanation for some; likewise is the disproportionate growth during adolescence. But eliminating both of these, can we entirely ignore the histories so frequently obtained?

In this connection, I am going to read the abstract of the paper which Levine of Boston is giving at the American Heart Association Meeting: "Recent years have seen concentrated interest in the streptococci as a possible cause of rheumatism. Recognizing the importance of this work, clinical experiences indicate that changes in the internal environment of the host must play a very significant rôle, and this aspect of the problem has received little attention. The strong familial factor which cannot entirely be explained on the basis of contagion and external environment suggests an inherent vulnerability. There is much we observe that points to changes in the endocrine balance as a factor in deciding whether an individual is vulnerable to this disease. The term 'growing pains' has more than colloquial meaning when the problem is viewed in this light, for thus it may be related to the endocrine system. It is also curious that chorea practically never returns after the age of twenty except under one circumstance, pregnancy. Here again the endocrine system is altered. Furthermore, there are frequent instances in which recurrent rheumatism appears in the same individual the same month of the year, particularly February. We now know that the weight of the endocrine glands alters during different months, and in February some of them are at a particularly low ebb. This may be a fruitful field for investigation."

Back in 1909, Sir Norman Moore said: "It would be very much more accurate to regard the carditis as the center of the infection and polyarthritis and chorea as complications. The joint lesions attract immediate attention by the pain they cause; the movements of chorea are not likely to escape notice; but it is the cardiac lesion which shortens life." All of us, I am sure, have had this dictum exemplified in practice, and further discussion of this phase would seem justified.

The mention of pneumonitis in association with rheumatic heart disease should stimulate an expression of opinion regarding the posterior lung findings in pericarditis. Certainly these findings cannot be entirely explained on the basis of effusion or compression. The clinical course prompts me to conclude that we are dealing here with a pneumonic process due to adjacent pathology.

Dr. McCulloch makes the statement that "during adult life the joint pains occupy a much more prominent part"—and further—"It is also well known that the chance for the heart to become involved during adult life is much less than during childhood." I have frequently been impressed with the same fact in children. In other words, when the arthritis symptoms were most prominent and fulminating, the milder was the resulting carditis. Is it that the infection spends itself here and thus lacks the potency to invade other susceptible structures?

The influence of race on the manifestation of rheumatic fever is sufficiently covered by Dr. McCulloch's concluding statement in that studies tend to show that "race is less of a factor than location." I would, however, raise the point that in my experience the Italian child with heart disease shows the most remarkable comeback of any race I encounter. Likewise, that the Negro race, even in the North, seems less vulnerable to the rheumatic infection.

Much has been said regarding specific phases pertaining to the rheumatic state in childhood, but the most important point to me is the social status of the patient. Were it and its contingent factors explained, I am sure we could forge ahead with one of the most striking examples of preventive medicine known in history. Our success must lie in the prevention of heart disease among children, not its cure. If we could once analyze and explain these environmental factors we would begin to accomplish results. Why is there such a dearth of rheumatic heart disease in private practice, and why such an abundance in our dispensary groups? Does sensitivity, allergy and heredity explain all? Certainly no field of investigation could be more fruitful and helpful than further study of the environmental factors pertaining to the rheumatic state and rheumatic heart disease in children.

DR. McCULLOCH.—One of the main ideas in these conferences is for each of us to express his own experience and the opinion formed as a result of that experience. By this all of us learn what others are doing. We would like to hear from as many as care to discuss any particular phase of the presentation thus far.

DR. T. D. GORDON (GRAND RAPIDS, MICH.).—Besides the ordinary chorea, are there any other brain conditions which are considered as being rheumatic—meningitis, for instance?

DR. ROBERT A. BLACK (CHICAGO).—I feel that a great many headaches in children might be looked upon as rheumatic in character. I personally have never seen meningitis that I would say was rheumatic. We all see many cases of chorea which resemble a mild encephalitis. In fact, I think it is hard to differentiate a severe type of chorea from encephalitis.

DR. BACHMANN.—What prompted your question?

DR. GORDON.—A case I recently saw—a child who had rheumatism, and who in my absence from the city was taken to the hospital with meningitis—2,000 cells, mostly polymorphonuclears, but no organisms were found on six lumbar punctures. This boy made a complete recovery without other treatment than salicylates.

QUESTION.—Did you make cultures of the spinal fluid?

DR. GORDON.—Yes, and no organisms were obtained. I returned to the city after four or five days, and knowing the history of the case, suggested the treatment, and the boy made a rapid recovery without any residual signs from the meningitis.

DR. PHILIP ROSENBLUM (CHICAGO).—One should be very careful in interpreting a 2,000 cell count. The patient may have had an epidemic meningitis; that alone does not speak for rheumatic involvement of the brain. One might have rheumatism and also have a meningitis of other origin.

DR. J. A. HENSKE (OMAHA).—We had a severe case of involvement of the serous surfaces, the parietal pleura, the pericardium, and the knee joints, and apparently the mind was also affected. The patient rallied from a temperature of 105°, after several days of treatment. There was involvement of practically all the serous surfaces of the body. I wonder how often you see this type. It is the first I have seen in years at the University Hospital.

DR. McCULLOCH.—We have heard during the last several years of the finding and identification of rheumatic pleuritis. Since that serous membrane can be involved I see no reason why the meninges might not be involved as well—maybe as definitely as in the case you describe. If the pleural surface can be involved it would seem that all the serous surfaces of the body could be involved likewise.

DR. HENSKE.—Has there been a study of the spinal fluid of cases of chorea? We do know there may be an increased cell count in a number of infectious diseases.

DR. McCULLOCH.—I do not recall any special study of the spinal fluid of children in chorea, though it has been done undoubtedly.

DR. J. W. EPSTEIN (CLEVELAND).—I did lumbar punctures in sixteen cases of chorea in my pediatric service, and the cerebrospinal fluid was negative in every respect.

It is rather new to me to regard malnutrition as an etiologic factor in rheumatism. I cannot recall in my experience, which is probably not so extensive as yours, anything that would point to malnutrition as a predisposing cause in rheumatism. In fact, most of the rheumatic children who came under my observation had always been well nourished and of the robust type. In cases of rheumatic carditis examined in the Cardiac Clinic at Mt. Sinai Hospital in Cleveland, we always investigate the other members of the family. To our surprise, we have found that other children in the family, who had never complained of an ache or pain, had demonstrable cardiac lesions. This would seem to indicate the importance of the familial tendency to rheumatic infection, and I think this tendency should be more emphatically stressed than the factor of malnutrition.

As to the question of race, I should like to say that my experience leads me to agree entirely with the English observers that blondes are affected more often than brunettes. The Nordic races do show more tendency to rheumatic infections than the Italian or colored races.

DR. H. O. McMAHON (MILWAUKEE).—I would like to say that in the Milwaukee County Hospital we have had a considerable increase in rheumatic heart conditions and chorea, apparently not due to any marked malnutrition. Our system of feeding is very good, as good as any in the country, and many of these cases being brought in have not been produced by malnutrition. The weight gains have been fairly satisfactory.

DR. McCULLOCH.—The question of malnutrition as a secondary factor associated with the occurrence of rheumatic fever is very important. It is a subject which concerns the pediatrician very intimately. The care and routine we prescribe and advise for infants through the early period of life and later on for older children of preschool age should result in children who are healthy, who pass through the preschool age with a better resistance to the infections of that period and who show a lower incidence of rheumatism, tuberculosis and many other important diseases occurring in later life. This same factor may be our most important contribution to the prevention of heart disease. It is the very reason why we pediatricians place so much stress to parents on the need of extra care.

Body weight alone does not constitute a good criterion of malnutrition even when considered in relation to body height. The obese child is frequently as much malnourished as one who is underweight. We have seen many children with chorea who are fat but on close examination, it is easy to recognize that they are malnourished just as much as those who are underweight. Our impression is that chorea occurs in the obese type of older child more than in any other constant type. I seriously question whether rheumatic fever and especially the heart disease that goes with it will occur in a child who is in good nutrition. I do not mean that all children who are malnourished have or may have heart disease. It has been observed also that many tuberculous children are normal in weight and that the incidence of underweight among tuberculous children is very low but again in these studies, the sole criterion of malnutrition was underweight without regard to other manifestations of malnutrition. I think a full clear definition of nutrition would possibly help us a great deal in interpreting what constitutes malnutrition. There are certain other diseases like rickets in which the children are not always underweight but should be considered as malnourished.

DR. W. S. GIBSON, CHICAGO.—What are the criteria for the determination of malnutrition in children?

DR. MCCULLOCH.—That is a rather difficult question to discuss at this symposium and in so short a time. Nutrition is the state in which living matter exists at any given time, resulting from the various processes of metabolism. As well as one can define this state in living children under ordinary conditions, the criteria are: (1) an estimation of body weight with some other mass measurement in relation to body length or some other linear measurement using the many and varied tables that have been described for the establishment of normal or average ratios, making allowances for those influences which deflect the individual from the normal or average; (2) an examination of those parts of the body which are susceptible to nutritional changes and which are evident on ordinary physical examination; the various qualities of the skin, the amount, consistency and distribution of subcutaneous body weight and the size, tone and coordination of skeletal muscles; (3) by some knowledge of the child's history in regard to environment, type of feeding, intake of accessory food elements, reaction to infection and other general habits of play, rest, school, etc. Further than this the question becomes very complex and involves the determination of many points in metabolic and chemical laboratories.

DR. ALBERT D. KAISER (ROCHESTER, N.Y.).—I want to say something about growing pains in contrast to fatigue pains. I have been interested in growing pains, as to whether they are symptoms of rheumatic disease or whether they are all fatigue pains. I followed a number of children over a period of years with a history of growing pains and no other rheumatic symptoms. In this large group of children I found that 10 per cent of the children who had growing pains appeared later with some involvement of the heart, in most instances not severe. They had a mild cardiac involvement, yet severe enough to be classed in the group of children having rheumatic carditis. It is of course not certain that the growing pains were responsible for the cardiac involvement but it is suggestive that persistent growing pains are the result of an infection. I found that 8 per cent of the children examined in Rochester gave a history of growing pains. A higher incidence of growing pains has been reported from other cities.

I am not in absolute accord with the statement that rheumatism is influenced chiefly by the social environment. It plays an important part but another significant factor seems to be necessary and that is the element of infection. Those who have followed Coburns' work in New York have been impressed with his studies on

nurses, training in the Presbyterian Hospital. Before completing their course 30 per cent had developed some form of rheumatic manifestation. He concludes that it is not so much the change of environment for they had adequate food and rest, but because they were brought in contact with streptococcic infection which they had previously escaped. The incidence of rheumatic fever has been high in Rochester during the last two years. There has also been a high incidence of scarlet fever. It was found that many children who appeared with rheumatism had scarlet fever within the last three years and the cultural studies of the throat flora showed a high incidence of hemolytic streptococci. The evidence at hand seems to suggest that poor social environment plus contact with the streptococcus is a factor in the causation of rheumatism.

I believe the improvement noted in children sent to Porto Rico is due to the absence of streptococci in the throat. The streptococcus is probably the exciting cause of the disease but a susceptible host is necessary. The factor involved rendering the host susceptible is not known. It may be some enzyme or internal secretion that fails to function properly.

DR. J. R. GERSTLEY (CHICAGO).—I have always been interested in the subject of growing pains. Every child seems to have them to some extent. When Dr. Kaiser reported a history of growing pains in a large percentage of rheumatic children, did he have any controls?

Of course I realize that Dr. Kaiser's study was not one primarily of growing pains. These were reported as purely incidental findings. However, growing pains are such a common complaint that I believe we should be somewhat critical as to their significance. For instance, if Dr. Kaiser reports that 10 per cent of his cases of rheumatic endocarditis gave a history of growing pains, what percentage of a like number of children without rheumatism and endocarditis would give a history of such pains? If a number of much less than 10 per cent would be found, I grant the evidence would be in favor of a rheumatic significance to these pains. But I do believe there should be a control series.

DR. McCULLOCH.—In reply to Dr. Gerstley's question, we have seen children in the clinic with rheumatic heart disease, oftentimes in an advanced stage with no history of pain in the joints, growing pains or any other kind of pain. The difficulty we have had is to know how to classify in an intelligent way the various pains these children may have. It is well known that they vary a great deal in degree, location and in many other characteristics. The well-defined inflamed joint seen so commonly in adult life with the usual objective signs is relatively infrequent in younger children. Mention has already been made of the pain in the legs from flat feet and it may be pointed out again, the rather common pain in the legs from fatigue. These pains should not be considered either growing pains or rheumatism. The chief difficulty arises when a child is seen with tonsillitis, with signs of heart disease and with ill-defined pains in the extremities. Such pains are probably due to rheumatism and should be so interpreted. I would like to insist again that mere growth should not produce pain in any form.

DR. ROSENBLUM.—One thing I would like to ask, is about erythema multiforme associated with arthritis, as a rheumatic manifestation. This association is more frequent than we realize.

DR. McCULLOCH.—The list of manifestations of rheumatism as given is, of course, not complete. I agree with you that erythema is a fairly common sign.

DR. EPSTEIN.—Skin lesions are certainly a manifestation of rheumatism. I think you see them in children who have rheumatic nodules, if the skin is involved in some form by the rheumatic infection.

I hoped somebody would bring up the question of erythema nodosum.

DR. G. R. WEINFELD (CHICAGO).—In reply to Dr. Rosenblum's question, Swift pointed out that this was also a manifestation of very serious cardiac involvement. I have had about six cases under observation for about four years, who have had erythema annulare. One boy has had it for about six years. He has no serious cardiac complications. At one time it appears as a coincident manifestation, its intensity depending upon the intensity of the infection. Then for a time the dermatitis disappears and again he will have the dermatitis without anything else. In one child with a severe heart lesion an erythema marginatum has been present for a long time. The other day I saw another child who had an erythema marginatum but I had not noticed it until I saw him in a strong light. I doubt very much whether it is a proliferative lesion. It has more the earmarks of an allergic manifestation. I think it is important that we all understand what we mean by this lesion.

DR. ROSENBLUM.—Rheumatic peritonitis may occur, but surely not very often. The majority, if not all of the cases were associated with pericarditis. We know one of the first symptoms of pericarditis is often pain in the abdomen, and not infrequently they get to the surgeon first, who operates only to find a pericarditis later. We know these cases do not need operation. Surgeons usually justify their operation by stating there was a peritonitis. They never obtain positive cultures and all the cases heal without drainage.

I feel the majority of these so-called operated rheumatic peritonitis patients are just a mistaken diagnosis for beginning pericarditis. I question, too, the occurrence of real rheumatic pneumonia. I feel much as does Dr. S. Gibson about the etiology of rheumatism. There is probably a specific organism as in tuberculosis, with environment, diet, vitamins, climate, etc., only secondary factors.

DR. BACHMANN.—I think Dr. Kaiser mentioned a very important point, "exposure to germs." We see this frequently in the form of epidemics. I think there must be something else associated; that is, the lack of proper attention to minor infections. The children we encounter in private practice receive attention for minor ailments and thus evade serious trouble. In the dispensary group these are ignored. I have felt that the indulgent care toward these minor infections, especially exposure to streptococcus, plays quite an important part.

DR. J. H. WALLACE (OAK PARK).—All this confusion about some of these things prompts me to challenge Dr. Bachmann's optimism about prevention. There is a good deal of conflict of opinion about race and hereditary and climate. In discussing malnutrition, Dr. McCulloch thought the definition should be emphasized. I feel the same way about prevention. The preventive phase of the problem as I see it is the following through, in the prevention of the second attack or prevention of complications in the heart. If by prevention of rheumatism one means prevention of the first attack, I cannot feel the optimism of Dr. Bachmann since we are not agreed as to the exciting cause. It would seem that prevention, strictly speaking, would entail eliminating the predisposing factors—a rather gigantic task if it means changing racial and hereditary characteristics and bringing up the housing situation and hygiene of the lower social strata. One thing I might mention with regard to race and color is that it is very difficult to infect an African Negro with scarlet fever, and the Chinese are only slightly susceptible. This might have something to

do with the fact that they are less susceptible to heart disease, since immunity to one streptococcal infection seems to involve immunity to other strains of streptococci.

DR. BACHMANN.—My optimism is simply the desire to educate the layman with the facts about rheumatism. The average parent who comes to us today with a child with heart complications has no idea as to what that might have come from.

DR. WALLACE.—That is probably correct. We cannot prevent rheumatism, however, until we know more about it. We can prevent the second attack. Strictly speaking, so far as the prevention of rheumatism is concerned, I wonder if we know enough about it.

DR. BACHMANN.—I feel that prevention will come before the cure, however.

DR. GIBSON.—Dr. McCulloch has had control over his patients for a long time and I wonder if, after a number of years, these children have had definitely fewer recurrences than other children not so well cared for.

DR. McCULLOCH.—That is a hard question to answer. About five years ago, we reported the results of a study of a group of cardiac children who had been patients in our convalescent home. Much to our surprise, we found that the number of attacks of rheumatic fever in the children who had received such care tended to be rather high after discharge to their homes, in comparison with a similar group who had not been admitted to the convalescent home. We felt, however, that the child's general condition had been greatly improved and that when the subsequent attacks occurred, they were of shorter duration and there was less involvement of the heart. Our only explanation of this observation was that when the child returned to his previous environment, particularly if the environment had not been improved, exposure to further infection resulted in attacks of rheumatism because his susceptibility had not been altered. The study led us to believe that convalescent care was of value chiefly during the time the child needed to be in a more favorable environment and also in rendering him more able to withstand subsequent infections. It still seems to us that the prevention of rheumatism lies first, in creating healthy children through the application of the broad principles of pediatric care; second, in taking care of children properly when they have an acute illness and, third, to be sure they are well of any infection before they return to school. I think these things lie distinctly within the field of pediatric care and have no more relation to cardiac problems than they do to other forms of disease. In this way, we will be able to prevent a lot of rheumatism.

DR. J. C. McKITTERICK (BURLINGTON, IOWA).—I am inclined to agree with Dr. Wallace as to the importance of prevention. When a patient comes to me with swollen joints I know he has rheumatism. He complains of stiff legs in the morning, has low fever, and fatigue; this leads me to believe that the child may have rheumatic heart disease. But what will prevent it? Until more work is done in the prerheumatic stage I think we cannot get very far.

DR. KAISER.—Might I state our own experience. We had the same feeling that individuals with rheumatic disease had low calcium and cholesterol values. We studied the blood lipids in 75 rheumatic cases, and found normal calcium values and the cholesterol was well within normal limits. They were low in the acute cases but they were also low in pneumonia and scarlet fever, but with recovery they returned to normal. Dr. Clausen studied the vitamin A content and the carotene in the same group but found no striking relationship between the rheumatic state and a deficiency of this vitamin and provitamin.

DR. McCULLOCH.—Balanced feeding and proper dietary intake are, of course, important. A survey of the diet of many of these children shows a history of a predominating bread and butter diet with relatively little milk, meat, eggs and vegetables. The mother often explains that the child eats enough but "runs it off," which is, of course, not true. Unfortunately, this same explanation is offered many times by physicians for the malnutrition, underweight and fatigue which may be present. Activity should not produce malnutrition and it is probable that with satisfactory food and regulation of activity, the child would not become thin. The improvement following administration of foods containing abundant calcium salts and cod liver oil often demonstrates that the diet was defective.

We now come to the third part of our presentation—*The Care of Children With Rheumatic Fever and Heart Disease.* It should be clear to everyone that the care of such children depends on the period in the course of the disease in which the patient finds himself. It is probable that a lack of consideration of this important subject accounts for the widespread divergence of opinion which exists in the minds of most of us and for the unsatisfactory directions for care that most patients receive. Measures which are applicable at one time would be inappropriate at others. It is suggested that four important periods in the course of the disease should be considered: (1) The period of active infection; (2) convalescence; (3) quiescence; (4) when the process is healed or when it has disappeared and the patient is cured.

1. During the period of active infection, evidence of activity must be sought and recognized. The three important points of evidence would be active focal infection in tonsils, sinuses or in any location, fever and rheumatic nodules. So long as cervical glands remain enlarged, the tonsils show evidence of redness, edema, thickening and pus, or so long as the mucous membrane of the nasopharynx shows hyperplasia, redness, edema, etc., the patient must be considered to be in the period of active rheumatic infection. Also, so long as the body temperature remains above normal or shows extreme daily variations, the patient should be considered in the period of active infection. Leucocytosis and joint pains are of value when they are present to a marked degree, but in the usual child their absence or presence is not of great assistance in determining the period of infection. Rheumatic nodules, however, are definite evidence of an active infection and so long as they remain, it must be assumed that an active process is going on in the heart. During the period of active infection treatment should be directed toward the control of those manifestations present. It is important during this period to clean out foci of infection as soon as it is determined that the patient can stand the necessary procedures. The use of salicylates and other drugs relieves fever, joint pains, and many other toxic manifestations. It is also important during this period to provide rest for the body and heart as much as possible. This important measure cannot be overemphasized, even though it is briefly stated here. If congestive failure of the heart occurs during this period, it is of grave prognostic significance and should be a matter of first consideration. So long as the heart muscle is unable to do its work, it is futile to undertake other remedial measures.

2. It has always been difficult to decide accurately when patients are getting well and are convalescent. In a disease like rheumatism, where the symptoms and signs are so varied and irregular, it is very much more difficult than usual. Some of the difficulty arises from the fact that few criteria are available to determine accurately the absence of infection. It has been suggested that a normal temperature and heart rate, together with a good appetite, should indicate recovery from any infection. These statements should hold true for children with rheumatic heart disease. In addition, children should show no signs of fatigue, should be gaining in body weight and height, and should be free of active infection in tonsils and

elsewhere. Other criteria such as the absence of leucocytosis, changes in the heart signs, etc., are also easily applied to the individual child during the period of convalescence. Graduated return to normal activity and function should be undertaken. Whether or not this period is short or long will be determined by the degree of injury occurring in the heart and body during the attack. It must be pointed out that there is a tendency to err on the side of a convalescence too short rather than too long, and in case of doubt it is safe to delay the convalescence.

3. By far the largest number of children with rheumatic heart disease are found in a period of quiescence. While those under the care of a physician are generally in the period of active infection or are convalescent, surveys show that a very much larger number may be found in school and not under the care of physicians. This very important group needs careful study and control. These children will be found on periodic health examinations, at school, and when under the care of physicians for some intercurrent condition. It is an important group to recognize, since remedial measures will yield larger returns than in almost any other group under consideration. These children are not ill, but their health is impaired, the chances for a return of the rheumatic fever are good, and the ultimate prognosis for their reaching healthy adult life is poor. Educational measures by individuals, organizations and institutions will uncover a large number of these children.

Their care consists of a regulation of their daily routine so as to provide a proper balance of activity and rest. When possible they should be allowed to attend school or be at work, and to undertake jobs which are within the limit of their performance. Since most of these children are in Class I, they probably need more of an adjustment of their physical activity than a restriction of such activity. Such a program seems desirable, because it allows the child to live more nearly normal than when restricted in any fashion, and probably is of greatest value because such children must be fitted for their life work. Unless they can learn their limitations they probably become maladjusted both mentally and physically and acquire an unusual outlook on life as well as their inability to support themselves. It also is important during the long period when such children remain quiescent to provide proper measures for good general health. By this is meant proper food, proper amount of sunlight and fresh air for play and rest, and enough sleep, and the importance of a quiet environment must be emphasized. That this factor is of some importance is borne out by the high incidence of chorea in children living in congested, noisy sections of the city.

4. Evidence is available that children with rheumatic fever and heart disease may recover entirely, so that at subsequent periods no evidence of disease can be made out. A larger group definitely are known to live for long periods without recurrence of their rheumatic fever or heart disease. Many of these have been known to live throughout the remainder of a normal span of life, with full physical activity and earning power, with no further heart disease. While this number is relatively small in comparison with the total number of children with heart disease who die early, it is sufficiently great to warrant special consideration. This opportunity rarely comes to the pediatrician because the problems involved are a part of adult life. The part for the pediatrician to know, however, is that there is some reward to offer the cardiac child for carrying out the directions. Unless this reward can be pointed out, the child may have very little to look forward to and no incentive to carry out instructions. The probable chance of recurrence of a myocardial, endocardial or pericardial lesion is always great. Such children must be treated more carefully when infections occur than individuals who have not previously had attacks of rheumatic heart disease. They must be told they will always require special protection. Children suffering from mitral valvulitis particularly when stenosis has occurred, have a bad prognosis, and Cotton has shown that 90 per cent

of such children are dead after a period of ten years from the onset of their disease. Contrary to the usual prognosis of patients with syphilitic aortitis and aortic insufficiency, when the prognosis of life is not greater than three to five years, children with rheumatic aortitis and aortic insufficiency uncomplicated by mitral stenosis seem to live and do well, provided the active infection disappears. It has been pointed out by Dr. Conner that such individuals may live several score years without cardiac distress.

DR. BACHMANN.—On the care of children with rheumatic fever and heart disease I am sure we are all agreed. Agreed at least so far as fundamental principles are concerned, though we may disagree on details. However, until facilities are generally available where patients with the varying degrees of rheumatic infection can be cared for, complete success cannot be obtained. My feeling is that the chronic cardiac cripple receives too much attention, while the milder types and those still considered potential receive too little. The only solution to this question rests in the establishment of more homes or sanitariums for the chronic or perpetual rheumatic, thus making available for the others more beds and more extended care. I find myself frequently discharging patients with a promising future and retaining those with none—only because the ward is crowded and something must be done about it.

In ascertaining when the acute stage of rheumatism has subsided, I feel that no greater display of the art of medicine exists. We all have clinical criteria upon which we pin our faith, but upon final analysis experience, observation and intuition are the factors which guide us most. Among the more recent criteria pronounced as valuable, is that of Bernard Schlesinger in a study of the sleeping pulse rate in rheumatic children. I would like to inquire if any of you have used this method and how reliable it has appeared to be. Personally, I attempted it but gave it up before a definite conclusion could be reached. To me the most convincing evidence of heart improvement and integrity whether in the hospital or in the clinic, has been weight maintenance and gain. No other functional test, in my experience, is more easily obtainable or more reliable.

DR. BLACK.—In answer to Dr. Bachmann's reference to Dr. Schlesinger's observation on the pulse change between the sleeping child and the child awake: Dr. Schlesinger showed many cases in which his night and day pulse ratio proved the correctness of his statement. At La Rabida Sanitarium we found it to be correct but it was not observed as frequently as Dr. Schlesinger seemed to find. We take a midnight pulse in the Sanitarium and find in chorea the reverse is true: in chorea a very high day pulse with a low night pulse; the spread of the pulse rate becoming much less as the chorea improves.

Dr. McCulloch does not feel as enthusiastic about the Sanitarium as I do. We have had about 1500 cases go through the Sanitarium. We do not have as good a follow-up system as Dr. McCulloch has.

The physicians treating tuberculosis made great advance in arresting the disease when they instituted sanitarium care. At La Rabida Sanitarium we have adopted much the same régime as is followed in a tuberculosis sanitarium: High caloric feeding with much rest and carefully supervised exercise. Until we know more about the etiology and specific treatment of rheumatism I think we would do well to stimulate sanitarium care. You educate the child and the parent as to the true nature of the disease. You are able to detect the slight relapses. Slight upper respiratory infections are often followed in seven to twenty-one days by a recurrence of rheumatism. A rheumatic child who has a slight upper respiratory infection would, in my opinion, be much improved if kept in bed until all symptoms disappear which is usually between two and three weeks. Do you not think that by such treatment the later mortality would be much lowered?

DR. GERSTLEY.—I, too, have been trying the Schlesinger test on cardiac children. Those who are recovering seem to have diminution of the pulse rate at night. On the other hand there are a number of fallacies in that test. When you ask the nurse specifically to take the pulse, she is likely to go at it so energetically that she wakes up the child. You must be sure that the child is asleep when the pulse is taken. Whether the interpretation of the drop in the pulse means that the infection is over is another question.

DR. BACHMANN.—It seemed to me that the count of ten which is supposed to be the difference between the alert pulse and the sleeping pulse, is too narrow a margin to be reliable.

DR. WEINFELD.—I wonder whether Dr. Kaiser would tell us about his experience at Rochester with tonsils. I would like to ask if there have been any ill effects from the removal of tonsils at the improper time.

DR. KAISER.—Personally, I am opposed to it, and so it has been done only occasionally. I believe the results are unfavorable. I do not have the data on that.

DR. WEINFELD.—When do you feel that tonsils should be removed?

DR. KAISER.—I have been interested in the relation of tonsils and rheumatism. I remember the old textbooks said that the way to prevent rheumatism is to take out the tonsils. When the opportunity came to observe a large number of children that was the first thing I studied, and in my opinion there is no great relationship between tonsils and rheumatism. The important thing in favor of tonsillectomy is that a great number of children are spared throat infections by having an early tonsillectomy. Again, statistics are very misleading. We have tried to approach the study from all angles in comparing a large number of children over a long period, those who were and those who were not tonsillectomized. We found 30 per cent less rheumatism in those who had been tonsillectomized—that is, 30 per cent of those children were protected against rheumatism. On the other hand, when we studied the children who had rheumatism, mild or severe, and were tonsillectomized, we could not prove a thing. However, that is my personal experience. I have a letter from Dr. Poynton in which he states he could not prove that tonsillectomy had any bearing on rheumatic attacks, but clinically he saw so much difference that he recommended tonsillectomy. I think I feel the same way.

DR. McCULLOCH.—We have been interested in a problem that is related to tonsillectomy. We have noted occasionally that a child who is either convalescent from or quiescent after an attack of rheumatism, within a week or ten days after operation for the removal of tonsils and adenoids will have an attack of rheumatic fever or chorea. Following the suggestion of Dr. Cameron several years ago, we instituted the procedure of giving salicylates before operation and continuing them daily for a week or ten days afterward, the idea being that salicylates would probably prevent in some way the rheumatic fever attack following tonsillectomy. It seems to us that the children do not react so much when salicylates are administered in this way.

QUESTION.—How do salicylates act in preventing the attack of rheumatic fever?

DR. McCULLOCH.—I do not know. Nor is it known how they affect any manifestation of rheumatism.

DR. EPSTEIN.—The chairman did not go into detail concerning the manner of administration and the dosage of salicylates. I get satisfactory results by

giving large doses, 150 grains, per rectum, and repeating when necessary. I should like to ask whether this method is preferable to administering smaller doses orally over a longer period of time.

DR. BLACK.—In cases of active acute rheumatism I give from 40 to 60 grains of sodium salicylate by rectum for three to five days, then continue with 3 to 10 grains three times a day for six months.

DR. A. L. NEWCOMB (CHICAGO).—I cannot help but wonder when we talk about prevention of rheumatic fever if treatment and prevention are not much alike. Physicians do not see the children much in rheumatic fever. The parents call up and directions are given to put them to bed, and usually salicylates are given. Sometimes the mother says, "I have you every time she has a temperature, yet here is a neighbor child who is playing out in the dirt and mud and is never put to bed with a cold." Yet it is the neighbor child who develops rheumatic fever. I am usually very careful as to how soon the child is allowed to get up. If the parents did not call for medical advice the children would be up and around in a few days. It is hard to separate prevention and care of the rheumatic state.

DR. MCCULLOCH.—We now come to the fourth article—*The Relationship of Rheumatic Fever and Heart Disease in Children to Heart Disease in Adult Life.* This important question has not been solved. Even the usual heart specialist is not familiar with the initial stages of heart disease in children, nor does the pediatrician frequently have an opportunity to observe his patients over long years into adult life. The evidence at hand today is chiefly of the "put together" variety, and is very unsatisfactory. It would be desirable if a large group of physicians, particularly pediatricians, could observe patients in adult life whom they have studied as children, and in this way learn something of the late effects of heart disease. The following points may be mentioned for discussion:

1. It would be important to note the number of adults with healed rheumatic heart disease who show recurrences of activity. It was suggested by Dr. Morse that chronic cardiac valvular disease should not be considered as rheumatic heart disease, and that an individual who once had rheumatic heart disease may lose all evidence of rheumatism. However, the nature of the heart disease is such that its etiology can usually be recognized, no matter at what time of life the patient is seen. It is true that when the active infection in the heart and the rest of the body has disappeared, the process in adult life is not similar to that seen in childhood, and presents the picture usually described as chronic cardiac valvular disease, but the origin of the lesion is rheumatic. Proliferative lesions of the aortic and mitral valves are always important, and when destructive changes in the heart muscle have taken place, an injury of a permanent type results. No matter at what period of life the patient may be seen subsequently, he will always tend to show characteristic signs and tendencies in the course of the disease.

2. Subacute bacterial endocarditis occurs most frequently in young adults who have either a congenital malformation of the heart or, more frequently, an old healed or inactive rheumatic heart disease. Indeed, a question has been raised as to whether an individual whose heart is normal would ever acquire subacute bacterial endocarditis. There is very little evidence to support such a supposition. Certain investigators believe that the differentiation between subacute bacterial endocarditis and rheumatic heart disease is not great and that they are the same process. The more general opinion, however, is that they are distinct processes, and the subacute bacterial endocarditis is superimposed on the old healed rheumatic heart disease. The usual organism involved in such an endocarditis is the *Streptococcus viridans,* though instances of staphylococcus, meningococcus, gonococcus and pneumococcus infections have occurred. It should be pointed out that in young adults with a

history of a rheumatic lesion who have fever and signs of infection, this important form of heart disease should always be considered. It is the usual cause of cardiac death in patients with congenital cardiac malformation, who are free of congestive failure.

3. Myocardial failure during adult life as a result of intercurrent infections or physical strain, particularly during athletic activities, may bear a definite relationship to an old myocardial injury received from a rheumatic infection or from other similar infections, such as scarlet fever, pneumonia, influenza and possibly from diphtheria. There seems to be little evidence that congenital syphilis affects the heart in such a way as to be responsible for myocardial failure in later life. Dr. Warthin, however, pointed out that sudden death may occur in adult life as a result of a congenital syphilitic infections. This idea has not been borne out by other investigators. The evidence available today suggests that most heart strain occurring in adolescence and early adult life can be traced directly to a history of rheumatism or other similar infection. Investigation of this relationship between the two periods of life should yield important information that would be useful to the pediatrician in directing a child who has had joint pains with or without heart disease.

4. Coronary heart disease which includes coronary thrombosis, infarction and occlusion, may occur as a result of circulatory changes in the heart muscle and vessels or as the result of senile changes going on in the body; but it has been suggested that these changes occur more frequently in individuals who give a history either of a high incidence of heart disease in the family or of rheumatic fever or a similar infection during early life. Coronary thrombosis may be a circulatory accident occurring more frequently in obese individuals under great mental and physical strain and bears no relationship to previous heart disease. Since coronary heart disease is an important cause of death, in adult life and particularly among individuals in the higher walks of life, it would seem important to determine the relationship between it and heart disease during childhood. At present this relationship does not seem to be very close.

Pediatricians have a large part in the prevention of rheumatic fever, by seeing that children are properly fed and cared for through childhood illnesses, and the mothers become intellectually rich if not financially rich through what we are able to tell them. It is a matter of intellectual status rather than economic status.

DR. BACHMANN.—I would like to emphasize, in conclusion, one factor regarding the pediatrician, not only in relation to heart disease, but also other chronic ailments of childhood, to say nothing of adolescence. We must extend our range so far as age is concerned. Without this we can never estimate the relation of rheumatic fever and heart disease in children to heart disease in adult life. Neither can we understand the influence an early nephritis has upon the adult. Nor will the adolescent boy or girl receive the intelligent support and guidance so highly necessary at this period. We need adolescent wards, dispensaries and physicians, and it is up to us as pediatricians to demand this extended service and prepare ourselves to handle this now neglected field.

DR. McCULLOCH.—Doctors particularly interested in rheumatic fever and heart disease who have had the opportunity to follow these rheumatic individuals from childhood into later life are very rare. When the child has been under the care of a general practitioner, he has either overlooked the relation entirely or has failed to recognize the heart lesion. As a rule the information we get from any source is not reliable.

DR. BACHMANN.—At the present time I am having that opportunity, but I am afraid that I have not been following them long enough to present data of

real value. After the patients leave the Children's Memorial Hospital I have been following them at St. Luke's dispensary to the age of eighteen or nineteen. The one outstanding thing I have noted is that the compensated mitrals and aortics in early childhood seem to have good tolerance and capacity until they get to about sixteen or seventeen, and then they suddenly die. That is the only striking thing I have been able to observe up to the present time.

DR. EPSTEIN.—I have not had this experience. The fact that about the age of twelve, children are transferred from the Pediatric Department to the Cardiac Clinic, makes it difficult for the pediatrician to follow cases through adolescence. I think that the only way we pediatricians can determine the subsequent condition of our patients, is by keeping our files, and inquiring from time to time as to the general status of their health. Recently Dr. Morse checked up by this method on one hundred cardiac cases which he had previously examined thirty to thirty-five years ago. In some clinics, especially in general hospitals which have cardiac departments, I think that it is a mistake to send these patients to the cardiologist. I would rather have the cardiologist come to the pediatric clinic, thereby benefiting by his suggestions and at the same time watching the progress of the patient.

DR. McCULLOCH.—Dr. Luecke, I would like to ask you a question. Is heart disease frequent in Dallas? and do you think it occurs among children living in western Texas?

DR. P. E. LUECKE (DALLAS).—I have been practicing there for about ten years and I have seen, I think, four or five cases of heart disease, and to my knowledge no important cases of rheumatic fever at all. I have seen growing pains and occasionally sore joints which probably were due to a mild rheumatism which rapidly cleared up without cardiac involvement. The cases of cardiac involvement I have seen have not been associated with rheumatism, and of the four cases that I recall of cardiac involvement, one occurred in a child about sixteen months old, who is now eight years old and the murmur is fast disappearing. He had no relapse. The second, in a child two and a half years old, ran a precipitate course and the child died in about four weeks. One other is on the Pacific Coast at this time. I saw him at about four years, off and on for five years, and he was subchoreic—highly nervous, with twitchings which were never choreic; the heart was never compensated; the pulse was slow. I do not recall the details of the fourth case. We do not see many cardiacs in the hospitals there and do not have the problem of bed space taken up by chronic cardiac cases. I have seen three cases of paroxysmal tachycardia in youngsters, which we thought due to repeated nose and throat infections—bad tonsils. After tonsillectomy they gradually improved. I have not heard from them for the last two or three years and do not know what developed. I do not know whether that had any effect on the rheumatic infection. The cases of rheumatic fever and heart involvement are comparatively rare.

DR. McCULLOCH.—Do you have many children with bad tonsils?

DR. LUECKE.—I saw one the week before I came up, but we do not see many.

DR. McCULLOCH.—I am always very much interested in hearing someone from regions of the United States like Texas, as to whether these conditions occur in those regions and to what extent.

The meeting adjourned at 4:45 P.M.

News and Notes

Following the diagnosis of chronic lead poisoning in a patient at the Children's Hospital in Boston, a study has been made for the source of the lead. An examination of the water supply of the house in which the patient lived showed that the connection to the street water main was by a one-inch lead pipe, approximately 100 feet long with house service of brass pipe. This finally led the Commissioner of Health to make a further study of water systems throughout the city and community. It has been shown that there still is in use a very large amount of lead pipe which has not been replaced by other material under present requirements. It has been observed also that the method of chlorinating water in the city has tended to release lead from old pipes which have been thoroughly coated from long use. These findings show that the water which most of the people of Boston are drinking contains a fairly large amount of lead. The importance of these findings is clear. It is probable that similar conditions exist to some extent in other communities. Recent publications from the Children's Hospital in Boston on lead poisoning should serve to point out this condition as an explanation of various anemias and diseases that occur in children. It should be pointed out particularly that the increasing density of the extremities of the long bones made out by x-ray examination affords an excellent means of diagnosis.

During the months of August and September, there has occurred in the St. Louis district an unusual epidemic of encephalitis. The epidemic started abruptly reaching a peak within three weeks' time, when about thirty to forty cases were reported daily. As this Journal goes to press, there has been an abrupt falling off in the incidence of new cases. The epidemic has been unusual in that the disease has been mild, except in patients above the age of forty-five who have already existing structural changes in various organs, notably the kidneys, blood vessels and heart. The mortality from encephalitis has been high in this group of individuals. Children of all ages have developed the disease though the incidence in the total number is relatively low. The mortality in this group has been especially low and at present it seems that most patients recover without residual effects. The disease in children has run a mild course, lasting a week or more with the usual signs of mild encephalitis.

With the very active assistance of the United States Public Health Service, the disease has been studied carefully from many different angles. It has been reproduced in laboratory monkeys into the second generation. No other important observations on either etiology, mode of transmission or treatment have been made.

The first annual scientific meeting of the **Georgia Pediatric Society** will be held October 12, 1933, at Atlanta. Dr. Arthur F. Abt, of Chicago, Dr. Horton Casparis, of Nashville, and Dr. Charles G. Kerley, of New York, will present papers on the program.

The Texas Pediatric Society held its last business meeting in Fort Worth, Texas, on May 9, 1933, at which time the following officers were elected:

Dr. Sidney Kaliski, San Antonio, President
Dr. Ramsey Moore, Dallas, Vice-President
Dr. Frank Martin, San Antonio, Secretary-Treasurer

The next scientific meeting is to be held in San Antonio on October 28, 1933.

The Governor of Tennessee has appointed a Public Health Council, two members of which, Dr. E. C. Mitchell of Memphis and Dr. Owen Wilson of Nashville, are pediatricians.

The Annual Meeting of the British Pediatric Association took place at Windermere on May 5th and 6th of this year. The President was Dr. Dingwall Fordyce. The scientific program was interesting, and the papers, of which only a few can be mentioned here, provoked in general very good discussions. Dr. A. V. Neale, in recording his observations on 300 fatal cases of tuberculosis in childhood, emphasised the important point that, in the case of young breast-fed infants who became infected, the fathers who were themselves affected with tuberculosis far out-numbered the mothers suffering from this disease. Dr. J. C. Spence gave an interesting communication on familial periodic paralysis; Dr. Lightwood and Dr. Hawksley spoke on icterus neonatorum gravis, and Dr. Ewart, in a paper on the treatment of rhinitis due to the Klebs-Loeffler bacillus, gave his experiences with x-ray therapy, which in his hands has proved extremely successful. Further, there was a general discussion on the prevention of ward infections.

On June 17th the **Children's Section of the Royal Society of Medicine** held its annual provincial meeting at the Children's Hospital, Birmingham. The clinical cases shown, and the discussions that followed, were of the greatest interest. Dr. Parsons and his colleagues at the Children's Hospital had assembled a magnificent array of cases for demonstration. That evening, a dinner was given to Dr. Parsons and Mr. Seymour Barling by their colleagues, to celebrate the production of the textbook on *Diseases of Infancy and Childhood*, which had appeared on the first of that month, and of which they are joint editors. Many of the contributors to this publication were able to be present. In the speeches following the dinner, great appreciation was shown of the work of the editors, who in reply expressed their indebtedness to the contributors, both from this country and from abroad.

On July 20th the **Third International Pediatric Congress** opened in London, at the British Medical Association House. Dr. Still was President, and we had the good fortune to be honoured by the presence of Their Royal Highnesses the Duke and Duchess of York. The Duke of York made an apt speech in opening the Congress, which was replied to by Dr. Still and Sir Thomas Barlow. As the record of the scientific proceedings, both papers and discussions, will be printed in full in the *Proceedings of the Congress*, I do not propose to go further into this aspect of the Congress, beyond saying that the general consensus of opinion was that it was highly successful. A feature of interest and favourable comment, however, was the excellent clinical demonstration at The Hospital for Sick Children, Great Ormond Street, of cases collected from various children's hospitals and clinics throughout London. On the social side one must first mention the President's reception at the Goldsmiths' Hall. This function was magnificent, and we were all grateful to this renowned old City Company for the hospitality they offered in their historic

and beautiful hall. The official dinner of the Congress was held at the Mayfair Hotel, speeches being made by Sir Hilton Young—the Minister of Health—Dr. Still, and Sir Thomas Barlow. After this function the Government gave a reception at Lancaster House, now the London Museum, which formed the setting for a very beautiful and impressive scene. The guests were received by Sir Hilton Young, on behalf of the Government. The Royal College of Physicians had an afternoon reception, the President, Lord Dawson, receiving the guests, and Lord and Lady Howard de Walden kindly entertained members of the Congress at tea in their home, Seaford House. Sir Gomer Berry and the Board of Management of the Infants' Hospital, Vincent Square, gave a reception in the hospital, and afforded an opportunity of viewing the beautifully arranged new wing just being completed.

Dr. George F. Still is retiring shortly from his hospital engagements, and it has been decided to recognise his retirement in an appropriate fashion. It is proposed that a cot be endowed and named after Dr. Still at King's College Hospital, where he has for so many years worked as physician in charge of the Children's Department; Mr. Gerald Kelly, an eminent artist, has promised a portrait of Dr. Still, provided that a certain specified sum be subscribed for the cot. Dr. Still, who was President of the International Pediatric Congress in London this year, is, as is well known, a pioneer of pediatrics in this country, and his retirement from hospital engagements will be deeply regretted by all his colleagues.

The British Medical Association held its annual meeting this year in Dublin. Dr. T. Gillman Moorhead, Regius Professor of Medicine at Trinity College, Dublin, being this year's President. Dr. Eric Pritchard was President of the Children's Section. The meeting was a great success, and our Irish colleagues exceeded even their usual great hospitality.

KENNETH TALLERMAN, London.
September 11, 1933.

Comments

THE relationship between pediatrics and the "Child Guidance" clinic and movement is gradually reaching a sound and satisfactory basis. Viewed from a broad educational standpoint the child guidance movement has been a success, as it has brought needed emphasis upon the importance of the child's behavior and emotional adjustment as well as the physical side of his development.

While the value of the "clinic" as a propaganda and educational measure cannot be questioned, the maintenance of such an organization as a distinct and separate entity, divorced from the established fields of medical activity except in certain specific situations, is neither logical nor sound. The make-up of such an organization composed of a pediatrically minded psychiatrist, psychologist, and social workers has proved its value. Such a group attached to a school system for the study and handling of children with educational problems is desirable for every school system where the value of its potential service is commensurate with the cost.

To set up such an organization as an independent medical unit is quite a different matter. To begin with, the vast majority of behavior and emotional problems, particularly those of young children, are not in themselves potentially psychiatric, and thus elaborate study and treatment by such a group is not only unnecessary but entails a cost in time and money which cannot be justified. On the other hand in many older children conduct and educational problems arise which require a detailed study and treatment that can only be given by such an organized group as the child guidance clinic.

The minor, or less important, guidance problems and particularly those of the younger children are distinctly pediatric problems. These should be handled in a routine way by the physician and the emphasis should be on their prevention. It is much easier to prevent a behavior problem than to correct it, and the vast majority may be easily foreseen by the physician who is alert and has this phase of child development in mind.

That more serious problems will arise, however, is just as true as the fact that serious health problems arise in the child who has received competent medical supervision from the time of birth. These problems often call for services of the technically trained surgeon, otologist or urologist, for example, to make a correct diagnosis and to outline and carry out the required therapy. The child guidance clinic has a similar function in its own particular field. To separate such an organization from the rest of the medical body, however, is to limit its usefulness and value. Coordination and cooperation with the medical group as a whole is the best way in which the child guidance clinic may develop its influence as well as fulfill its opportunities.

The pediatric clinics as a whole are rapidly recognizing the importance of a special group within their organization for the handling of difficult conduct problems. This is the logical and sound place for a child guidance clinic. Where such a situation or "set up" has been created the rapidity with which the pediatric

clinic has become psychiatrically minded is amazing. What is more important than the work of a child guidance clinic per se, which can only look after a small fraction of the problem children and whose work is chiefly therapeutic, is the influence of such a clinic in the pediatric group. Thus situated its influence extends to medical student, house officer and graduate student. It is upon these individuals in the ultimate analysis that the prevention of behavior and conduct problems will depend.

The Journal of Pediatrics

CONTENTS FOR OCTOBER, 1933

Original Communications

Significance of the Water Metabolism in Health and Disease. Irvine McQuarrie, M.D., Minneapolis, Minn. ---- 539

Chronic Peptic Ulcer in Childhood. Charles Stanley White, M.D., F.A.C.S., Washington, D. C. ---- 568

The Serum Albumin and Globulin of Newborn, Premature and Normal Infants. Daniel C. Darrow, M.D., and M. Katharine Cary, A.B., New Haven, Conn. ---- 573

Management by Mechanical Respirator of Postdiphtheritic Respiratory Paralysis. J. E. Gordon, M.D., D. C. Young, M.D., and F. H. Top, M.D., Detroit, Mich. ---- 580

Neurocutaneous Syndromes in Childhood. Herman Schwarz, M.D., and Harold Abramson, M.D., New York, N. Y. ---- 586

Determining Appropriate Weight for Body Build. Helen Brenton Pryor, M.D., and Herbert R. Stolz, M.D., San Francisco, Calif. ---- 608

Hereditary Ataxia. Allan Penny Bloxsom, M.D., Houston, Texas ---- 623

Virilism and Hypertension in Infancy Associated With Adrenal Tumor. Frank van der Bogert, M.D., Schenectady, N. Y. ---- 629

The Treatment of Pertussis With Gold Tribromide. J. Epstein, M.D., New York, N. Y. ---- 635

Antiques of Pediatric Interest. T. G. H. Drake, M.D., F.R.C.P.(C) ---- 639

Critical Review

Tuberculosis in Children, Lee Forrest Hill, M.D., Des Moines, Iowa ---- 641

American Academy of Pediatrics

Proceedings Third Annual Meeting of the American Academy of Pediatrics ---- 654

News and Notes

News and Notes ---- 674

Comments

Comments ---- 677

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